

The Alan C. Woods Issue

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Reference: 1. Hogan, M. J., Thygeson, P. and Kimura, J., *Arch. Ophth.* 53:165, Feb. 1955.



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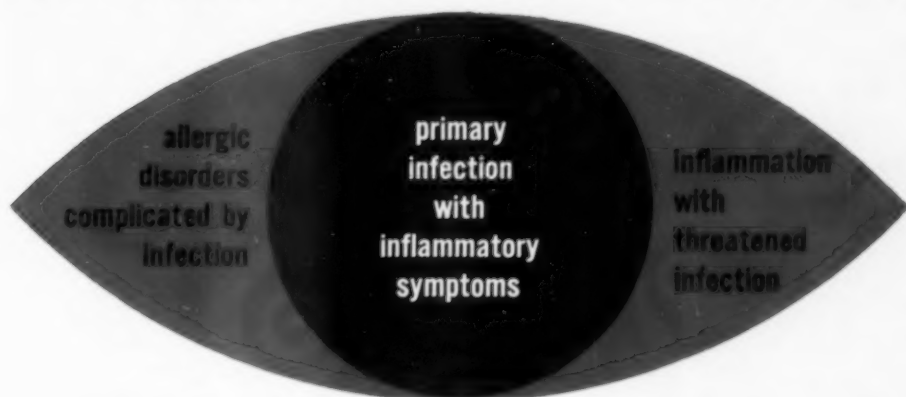


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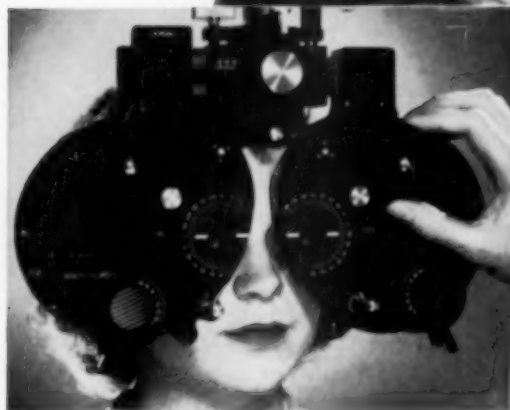
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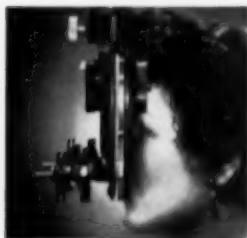
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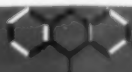
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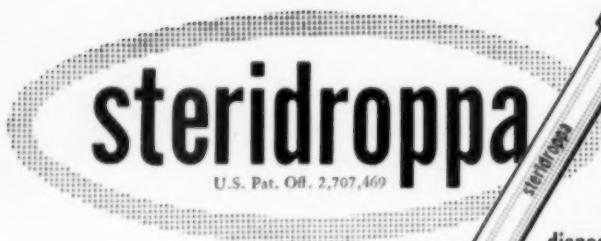


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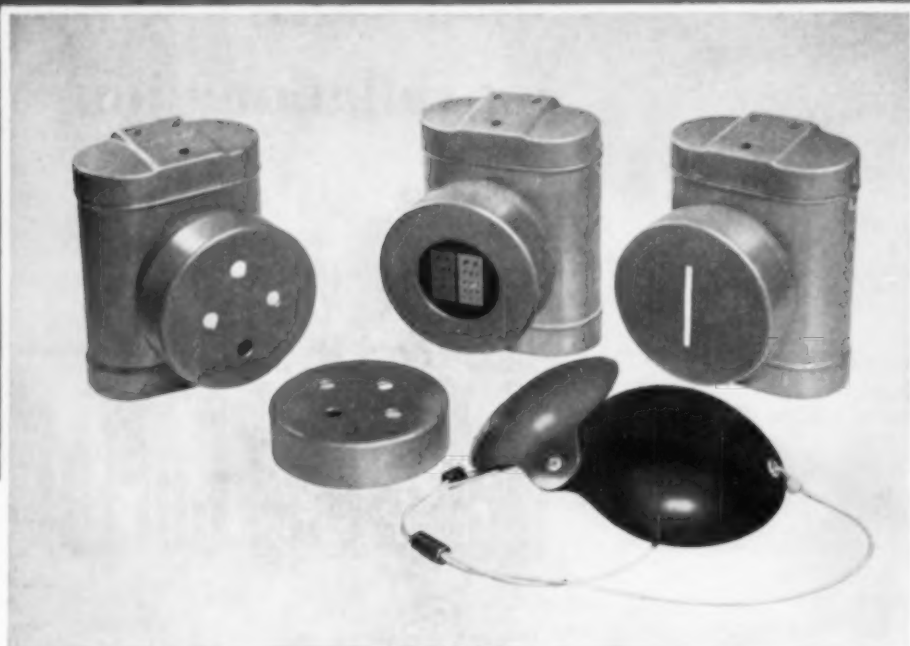
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*Schlagel, H. E., Jr., and Swan, E. C.: A. M. A. Arch. Ophth. 51:663 (May) 1954.

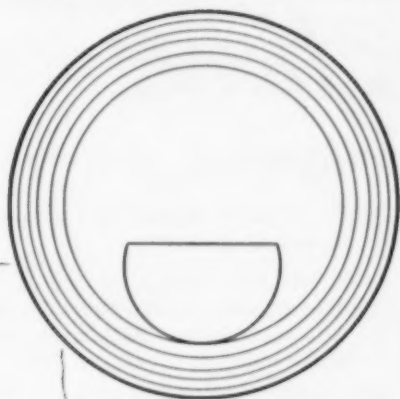


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1. Rasgorashek, R. H., and McIntire, W. C.: *Am. J. Ophth.* 40:34 (July) 1955.
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4. Gordon, D. M., and Ehrenberg, M. H.: *Am. J. Ophth.* 38:831 (Dec.) 1954 (a review of 8 studies covering 1035 patients).

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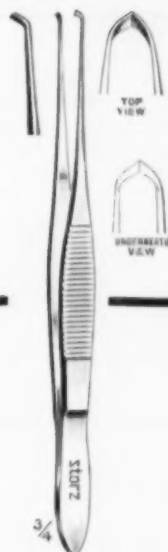
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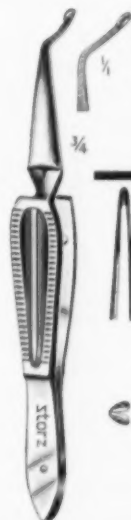


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AMERICAN JOURNAL OF OPHTHALMOLOGY

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THE ALAN C. WOODS ISSUE

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ABSTRACTS

Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous; Optic nerve and chiasm; Neuro-ophthalmology	559
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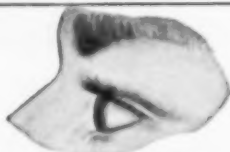
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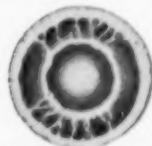
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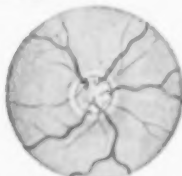
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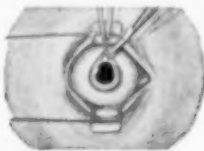
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ALAN CHURCHILL WOODS, M.D.

ALAN CHURCHILL WOODS, M.D.

M. ELLIOTT RANDOLPH, M.D.*

Baltimore, Maryland

That Alan Woods should become an ophthalmologist might have been taken for granted since his father, Dr. Hiram Woods of Baltimore, was an outstanding one. However, his father's influence had more to do with guiding him into medicine rather than ophthalmology. After receiving his A.B. from The Johns Hopkins University in 1910, at the age of 20 years, he seriously considered taking graduate work in English, leading to a Ph.D. and a teaching career. However, he cast these aspirations aside and entered The Johns Hopkins Medical School in the same year.

From the pertinent data at hand, his academic sailing seems not to have been entirely smooth during his first two preclinical years. History records that anatomy was certainly not one of his favorite studies, and it is noted with fair authenticity that, during a chemical experiment, he almost blew up a wing of the chemical building and, with it, the beloved and eminent John J. Abel, the crystallizer of insulin. Had he not gained later fame in ophthalmology, he might have been known to posterity for this alone.

His last two years in medical school saw his interest turn to internal medicine, and upon his graduation in 1914, he became a House Officer in Medicine at the Peter-Bent Brigham Hospital in Boston. He states, if I remember correctly, there was only one married man on the resident staff. The balance of us wallowed happily and economically in sinful celibacy!" Here he came under the influence of Dr. Henry A. Christian, who stimulated his interest in research bacteriology. The following year, he entered upon a two-year fellowship at the University of Pennsylvania. Here, under the guidance of Richard Pearce, Professor of Research Medicine, he became more and more interested in re-

search pertaining specifically to ophthalmology. While he held this fellowship, he wrote about 14 papers dealing with his particular interest—allergy and immunity—subjects which today are still his prime focus. Realizing that his training had been purely experimental, he decided to learn more about the clinical side of ophthalmology and was given the opportunity of spending the afternoons working with Dr. George E. deSchweinitz.

In Boston, a few years earlier, an enthusiastic recruiting officer had induced him to join the Medical Reserves. Apparently, his impetuous act had been completely forgotten, and he was severely shocked in 1916, while still in Philadelphia, when a letter arrived from the Adjutant General ordering him to Mexico as a first lieutenant in the Medical Reserves. This mission, which lasted about five months, was relatively fruitless, both for the country and for Dr. Woods, although he did manage to turn out a paper on tuberculosis while he was stationed at a hospital in New Mexico.

After his encounter with the Army, he completed his second year at the University of Pennsylvania and then returned to Baltimore and married Ann Powell Byrd of Gloucester County, Virginia. It was planned that they should live in Baltimore and that he should become an office assistant to his father, but World War I had started and he was asked to join the University of Pennsylvania's Medical Unit as a captain. He was placed in charge of the laboratory and sent overseas. Fortunately, Dr. deSchweinitz, then the Consultant in Ophthalmology for the American Expeditionary Forces, was able to pry him loose from his job and have him transferred to a British Army Group headed by Sir William Lister. Under the latter's guidance, he did a tremendous amount of eye surgery and learned more and more of the clinical side of oph-

* From the Wilmer Ophthalmological Institute of The Johns Hopkins Hospital and University.

thamology. He was discharged from the Army as a major in 1919, and he returned to Baltimore and worked as an office assistant to his father in the mornings and in the Eye Clinic of The Johns Hopkins Hospital in the afternoons. At that time he was Instructor, and later, in 1922, Associate in Ophthalmology. In 1925, the Wilmer Institute had begun and he served as Assistant Director to Dr. Wilmer. In 1926, he was made Associate Professor. He continued his private practice in the city, his father having died in 1931. When Dr. Wilmer retired in 1934, Dr. Woods succeeded him as Director and, at the same time, became Acting Professor of Ophthalmology. He made no drastic changes, and the routine of the Institute went on pretty much as usual. However, he soon began to take a more active part in the teaching program and to carry out his aims for graduate teaching. In his own words, "It is my firm belief that continued bedside instruction day in and day out is the best form of graduate training. . . . Thus the young graduate in medicine follows the patients through an illness, perceives the pitfalls of diagnosis, learns the good and bad results of therapy and operative interference, and finally wins through to his goal—the acquisition of clinical and surgical judgment. . . . Thus I believe that the foundation of graduate teaching should be bedside teaching, reinforced with lectures and seminars on various subjects."

Soon the administrative duties of the Institute and Hospital, in which he was a most active participant, became more and more time-consuming, making it increasingly difficult for him to maintain an additional office in the city. So, in 1937, he gave up the city office for the permanent office in the Wilmer Institute. In 1946, he became full Professor of Ophthalmology. Meanwhile, the pattern was being set for the active scientific life which he has since followed with little deviation throughout the years. His intensely vigorous routine has been the envy of a few and the consternation, exhaustion, and ad-

miration of many. One wonders how such a pace can be maintained—staff rounds, informal ward rounds, operations, private patients, student lectures, committee and board meetings, a voluminous amount of correspondence, afternoons in the laboratory, a dash back to his office, an hour or two of work on a paper, then home around 6:30. If not to dinner, medical or otherwise, he spends the rest of the evening with nonmedical reading.

As one of his ex-Residents, Dr. Samuel McPherson stated, "A working day with the Professor ordinarily began at 9:00 A.M., but it was usually wise for his assistant and the secretaries to arrive at least half an hour early in order to retrieve equipment which had been borrowed from his examining room by residents the previous night. This would avoid highly vocal accusations of theft which invariably occurred if a prism or lens was missing. Immediately upon his arrival, he would scan his appointment book and loudly scream that the secretaries had no right to fill up his mornings in this manner—forgetting, of course, that it was he who had scheduled the extra patients. If the day was busy, all notes were dictated; if it was not, the Professor wrote his notes in longhand. In either event, it was the duty of his assistant to translate his recorded voice or his completely illegible handwriting for the benefit of the secretaries and nurses. This was never a dull task, since he frequently had a unique way of expressing himself with some classical phrase or quotation.

"After a 15-minute lunch, he made rounds on his private patients. This usually required about an hour. This was followed by a trip to the animal room to examine the rabbits involved in the study of experimental ocular tuberculosis. The working day usually ended at 6:30, and by this time, he seemed pretty fresh, while his assistant could barely make it. We were all amazed at his capacity for work and glad that we had not been exposed to him when he was younger and more vigorous."

One also wonders how he ever had the patience to refract—yet refract he did—and in spite of the fact that his mind probably was on the antibody titer of the aqueous or some related problem in uveitis, those who inherited his routine refraction cases attest that while few such patients were honored with his small talk, his glasses were as satisfactory as the next refractionist's. On many occasions, it was a rewarding experience to overhear him refract, particularly if the patient happened to be not too intelligent or co-operative. If deafness was an additional shortcoming, a large and appreciative audience could be expected outside his door.

He has always been interested in sports. Although admittedly no richer for his excursions, he rarely misses one or two visits to Pimlico and Laurel each meeting. For years he was an ardent duck hunter and was said to have been better than an average shot. When an undergraduate at Hopkins, he played on the football team, and even when a first-year medical student, he was persuaded to help out the Varsity for its game with Jim Thorpe and the Carlisle Indians. The Professor admits he "lasted about six minutes." He still takes in many key games of football and baseball in the vicinity. A few years ago, he made the train trip to Philadelphia for the Army-Navy football game on a particularly wretched day. He was completely attired in his ducking outfit and was probably one of the few who remained both dry and warm, to the curiosity of his fellow passengers but to the envy of his fellow spectators. His absorbing hobby is fishing, and this is a daily routine during his summer stay at his home in Gloucester County, Virginia.

He is amazingly well read. In addition, he seems always to be working on two or three papers—allergy, immunity, ocular tuberculosis, and sympathetic ophthalmia have always been his particular specialties. The fact that each is highly controversial and has occasionally brought him into academic conflict with some of his colleagues only serves to

stimulate him further. His papers dealing with clinical and laboratory research, often in collaboration with Jonas Friedenwald, Alan Chesney, Earle Moore, Earl Burky, or later, Ronald Wood, are familiar to all ophthalmologists. His contributions have also covered the clinical aspects of ocular syphilis, chemotherapy, the steroids, neurology, and ocular surgery, all of which have been the subjects of well-planned, excellent papers.

On two occasions, he ventured forth as an ophthalmologic trouble-shooter. The first was in 1935 when he took issue with a proponent of the use of adrenal cortex for the cure of glaucoma. In a neat piece of clinical investigation, the Professor proved to the complete satisfaction of most ophthalmologists—and certainly to himself—that the cure of glaucoma was not to be found in the adrenals. These conclusions, however, seem to have come as a shock to the originator and were so unconvincing that a \$50,000 libel suit was slapped on the Professor. Nothing whatsoever ever came out of this, and after a few meetings with the opposing lawyers, the suit was withdrawn. It might be added that the process servers met him as he stepped down from the speaker's rostrum after a talk at the New York Academy of Medicine. He has said that the shock was similar to that he received when ordered to go to Mexico in 1916 (*vide supra*).

In 1952, he was Chairman of the committee appointed by the American Medical Association to investigate the cure of cataract by fish lens protein. Here again it was convincingly proved that such therapy for the cure of cataract was completely and utterly worthless.

In 1943, he wrote an outstanding article on the problem of the blinded casualty in World War I. As a member of the Subcommittee of the National Research Council, he called attention to the errors and mistakes made in the handling and training of the blinded casualties in that war and suggested plans to avoid these pitfalls in World War II. This paper made a resounding im-

pression on the medical authorities in Washington and certainly stimulated the founding in 1944 of the Old Farms Convalescent Hospital which became famous for the Army's Blinded Rehabilitation Program.

He is as meticulous and precise in the preparation of his own papers as he is insistent that those of his own staff conform to his standards of clear writing. Every paper originating from the Wilmer Institute is read by the Professor. To the tyro, and even to an occasional veteran, this can be quite an ordeal. It is usually around five in the afternoon when these sessions are held in his office. The Professor sits at his desk with the fresh, neatly typewritten manuscript in his hand. His invitation to draw up a chair and sit down is just another way of saying, "Hand me that stick, son, and bend over." A word, a phrase, a whole sentence, or even a paragraph will be rearranged, regrouped, or deleted. Occasionally, he may spend 30 minutes going over one page, with the author humiliatingly sweating it out beside him. After a particularly exhausting encounter with an obstinate paragraph, he will pause, light one of his vile-smelling, denicotinized cigarettes, and reminisce about the time he almost fired one of his residents because a key sentence failed to contain a verb! One resident recalls his saying, "No, damn it, no! Syphilis cannot be prevented by the way you have it written here! You are old enough to know there is only one way to prevent syphilis!" Another resident, after the Professor returned his literary effort, battle-scarred but still breathing, framed the first page and entitled it "The Anzio Beachhead, 1949."

In 1941, he began to notice blurring of vision in both eyes, and this turned out to be caused by rapidly developing cataracts. When the time came for surgery, he had so much confidence in his own residents that there was never any question in his mind who would do the operating—it would be that surgeon who had just finished his residency. It happened to be Dr. Jack Guyton, and his

confidence was completely justified. He got two beautiful, round pupil, 20/15 eyes. The long, anxious, postoperative days were particularly hard for him, and it is said that he violated every rule a cataract patient should follow. He was the cause, however, of the discarding of one great tradition at the Wilmer Institute—that of remaining flat in bed for a period of days following operation. As he lay there himself, he had ample time to philosophize and think about this problem. As Dr. Guyton said, "the answer, which came to him like a bolt out of the blue, suddenly appeared completely obvious; the patient should not lie in bed for seven days or four days or 10 days, but for zero days! Having reasoned this out, the Professor made of himself the first guinea pig for testing this most reasonable hypothesis." Dr. Guyton went on to say, "I vividly remember how relieved I was when I could tell him at the conclusion of his second operation, 'Professor, you are again symmetrical.'"

An ophthalmologist with aphakia is a rarity and he has since made the way easier for many patients facing this operation. He trained himself in manual dexterity and depth perception by working jigsaw puzzles and cleaning and picking hardshell crabs. A recent editorial in *THE AMERICAN JOURNAL OF OPHTHALMOLOGY*, "Adjustment to Aphakia," is known to us all.

He even experimented with contact glasses but this was a very unhappy experience. At an Academy meeting in Chicago he was persuaded to have them inserted in his own eyes. The fits were obviously imperfect, and the rapidly developing blepharospasm soon became so intense that it took the combined efforts of Drs. Maumenee, Constantine, and John McLean, augmented by speculum, lid retractors, forceps, and local anesthesia to remove them. "It was a rather rugged half hour," to quote the Professor, "much more unpleasant than the actual removal of the original cataracts." He readily admits that he may be "psychologically unfitted to wear contact glasses."

He has had a large and active surgical practice; yet one feels his first love was always medical ophthalmology. He has superb surgical judgment, somewhat conservative and never radical. He judges a surgeon's ability a good deal on the result rather than his actual technique. On ward rounds, he was certainly unstinting in his praise of an excellent operative result and sympathetically tolerant and helpfully analytical of an unfortunate one. He has been heard to comfort many a young surgeon with, "If you are going to do surgery, you are going to have to learn how to take the occasional bad result." It was always a pleasure to assist him with his operations, and he was always completely considerate of his assistant and the operating room staff. The term "operating-room prima donna" could never be used for him, except when he would sing "In the gloaming, oh, my darling" (slightly off-key), when doing a simple enucleation. The only real sign of irritation was the occasional tossing away of a pair of right-handed scissors, because of extreme left-handedness. On some occasions, the patient could match the Professor with repartee, and these encounters are well remembered. How vividly one recalls the Professor's comment at the finish of an uncomplicated cataract extraction. After he had said, "It's all over, and you are going to have a beautiful eye," to which the patient replied, "Thank God," the Professor rejoined with, "God had little, if anything, to do with *that* extraction!"

His Monday and Thursday morning ward rounds were particularly stimulating and, depending upon the number of cases, would last as long as two hours. A definite pattern was followed: The new case was presented by the intern who was directly responsible and, as the Professor once wrote "trivialities and false leads exposed, inadequacies in the histories filled in by direct questioning of the patient until presumably an adequate history was obtained." The intern was then questioned as to physical findings, diagnosis, and therapy. As Dr. Howard Naquin recalls, "It is an unforgettable experience in the

training at the Wilmer Institute. For the new House Officer, gamely attempting to parlay a few partially remembered facts, hastily obtained from Duke-Elder the night before, into what might pass for an intelligent answer, the opening question of the Professor, 'Whose patient is this?', was always terrifying. So were the succeeding ones. The questions that followed almost invariably led to the crux of the clinical problem at hand, the assistant residents, and resident, being asked their opinion, and finally the senior members of the staff. Meanwhile, the Professor would be examining the patient. This procedure would oftentimes add additional excitement to the proceedings, as he always wore a protruding loupe which miraculously never seemed to get in the other eye. After the questions to the staff, the Professor would sum up and give his opinion. He stated in an article on graduate teaching, 'errors in the ex cathedra judgment become apparent, and it is an inescapable fact that the staff learns as much and often even more from the mistakes and errors of the chief than they do from his vindicated judgment.'

When visitors were present, their participation in the discussions was always welcomed. It must be mentioned, however, that on one occasion the foundations of the Wilmer Institute were severely shaken when a distinguished foreigner made the unequivocal statement that, except for miliary tubercles, ocular tuberculosis simply did not exist!

While outspoken and critical of errors of omission and errors of judgment on the part of the resident staff, the Professor was equally lavish in praise of his staff in those particularly trying cases in which his kind words had an almost miraculous effect in restoring the confidence of both patient and surgeon.

Dr. Naquin continues, "His enthusiasm could never be suppressed when he encountered religion on the wards. Confronted with a patient whose faith in the Wilmer Institute did not preclude a visible rosary or two, the Professor might ask of the Resident, 'and what has this candidate for Heaven

got?' He was always careful to point out to visiting clergy that physicians and clergymen had fundamentally the same goal in life—to keep people out of hell—one temporarily and the other permanently. His opinion regarding some of the more dubious therapeutic agents was expressed in such an unforgettable phrase as, 'you're just flogging a sick horse.' Confronted with an eye that passed beyond the hope of living, the Professor's favorite expression was that of V. Gould—the eye had 'gone where the woodbine twineth.'

"It has been the common feeling of many of us who have accompanied him on ward rounds over a period of years that he has somehow 'mellowed.' This, I am convinced, is not the case. On the contrary, it has not been the teacher but the pupils who have changed. As only a teacher can, he has used his ward rounds to mold us skillfully as he would."

One of the most pleasant of his many committee positions was that as Chairman of the Sub-Committee in Ophthalmology of the National Research Council. According to a fellow member, Dr. Blake Dunphy, "the Professor was a master at running these meetings and had the ability to make the other members of the committee hew to the line. After a meeting was over and the policies decided upon, he would write a complete summing up in succinct and carefully worded sentences which were the envy of most of us." Following most meetings, adjournment would take place to his house in Baltimore for dinner. The Professor is noted as more than an average gourmet and a connoisseur of fine wines. These affairs were always long remembered by the committee for one or more pleasant reasons, but that he is not completely infallible in his wine taste is attested to by Dr. William Rienhoff who recalls with great delight how the Professor, at another dinner party, went into ecstasies over "the best Steinwein I ever tasted," which indeed was a disguised bottle of extremely flat champagne.

Many honors have come to the Professor.

His first prominent office was in 1947 when he was elected President of the American Academy of Ophthalmology and Otolaryngology. His presidential address, "Present Policy of the American Board of Ophthalmology and the National Societies in Relation to the Progress of Ophthalmology" candidly expressed his opinions in a fresh and sincere treatise. His views on these subjects, however, have not gone unchallenged. In 1948, he was awarded the Ophthalmological Research Medal by the Section on Ophthalmology of the American Medical Association. In 1953, he was the recipient of the Howe Medal given by the American Ophthalmological Society. He was made a Fellow of the Royal College of Surgeons (Edinburgh)—the only American ophthalmologist so honored in the history of the Society. He was also given an Honorary Doctor of Laws by Hampden-Sidney in 1951. As a lecturer, he has given the Jackson, May, Gifford, deSchweinitz, and the Proctor Lectures. In 1955, he gave the Lecture of the Guest-of-Honor at the American Academy of Ophthalmology and Otolaryngology. This again expressed his thoughts on a highly controversial issue in no uncertain terms, the repercussions from which have yet to die down. He is President of the American Ophthalmological Society for 1956.

At the age of 66 years, the year of his retirement, he returns to the Wilmer Institute as Emeritus Professor. Retirement is an imperfect word and ill fits the Professor. True, his administrative and teaching duties will be over, but one can be completely certain that he will work as hard as ever and keep the same terrific pace, except, possibly, in different channels. He has lived well into the period of his greatest activity, and it will never be like him to withdraw into an inconspicuous place in the contemporary scene. It is a happy thought to know that one of America's great leaders in ophthalmology will be with us for many more years.

11 East Chase Street (2).

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AQUEOUS HUMOR DYNAMICS*

THEORETICAL CONSIDERATIONS

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Editor's note: This issue would not be complete without a contribution from Dr. Woods' colleague and friend of many years, Jonas Friedenwald. This paper is presumably the last one upon which Dr. Friedenwald worked. It is reprinted here by permission from the *A.M.A. Archives of Ophthalmology*.

In a series of papers, Kinsey^{1,2} developed the technique of posterior chamber taps and has applied this technique both to the study of steady-state relations between plasma and posterior and anterior chamber concentrations of normal constituents³ and

to the analysis of aqueous humor dynamics as disclosed by the changing concentrations of a test substance in anterior and posterior chambers following the injection of such a test substance into the animal.⁴

To express the rate of change of concentration of the test substance in the anterior chamber, Kinsey and Palm have used the equation

$$\frac{dC_a}{dt} = K_f(C_r - C_a) + K_d(C_p - C_a) \quad (1)$$

where C_r , C_a , and C_p represent, respectively, the momentary concentrations of the test substance in the fluid passing

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through the pupil (π), in the anterior chamber (a) and in the plasma (p). K_f represents the rate of flow per minute as a fraction of the volume of anterior chamber; K_d represents the corresponding rate of diffusional exchange between anterior chamber and plasma. Thus, the rate of change of anterior chamber concentration dC_a/dt is expressed as the algebraic sum of inflow $K_f C_p$, outflow $-K_f C_a$, and diffusional exchange $K_d(C_p - C_a)$.

It is the purpose of the present paper to examine the factors involved in what, at present, can be considered required in any reasonably complete theory of aqueous humor dynamics. The analysis will proceed in two parts. In the first we shall consider the assumptions involved in Equation (1) and attempt to establish, if possible, the limits within which these assumptions are valid. In the second we shall show that under certain further limitations this equation may be integrated. The application of the integrated equation to experimental data furnishes a further test of the validity of the underlying assumptions.

Equation (1) is closely related to the expression originally used by Kinsey and co-workers in developing the theory of diffusion plus flow as applied to aqueous humor dynamics.^{5,6} In all preceding work, however, it had to be assumed for the purposes of simplification that the concentration, C_x , of the test substance in the fluid entering the anterior chamber via the pupil was constant so long as the plasma concentration was constant. Kinsey and Palm's new contribution consists in using posterior chamber taps as an assay of the momentary concentrations C_x . Even if fluid entering the posterior chamber contains a fixed concentration of the test substance as long as the plasma concentration is held fixed, the concentration in a mixed sample of posterior chamber fluid cannot be expected to be constant, because the volume of the posterior chamber is not negligibly small and time is required for its filling with the newly entering fluid.

Moreover, at the beginning of such experiments as Kinsey and his co-workers have performed the concentration of the test substance in the vitreous and lens is zero, while at the end of the experiment these concentrations must have reached some steady-state values. The building up of concentrations in these "posterior reservoirs" must occur in part at the expense of test substance lost from the posterior chamber. Thus, there are sound a priori reasons for expecting the posterior chamber concentration, and hence also the pupillary concentration of the test substance, to vary during the course of the experiment. Previous investigators have not been unaware of these complications. However, until the technique of posterior chamber taps was developed, such considerations could be of only theoretical interest.

PART I

1. LINEAR RELATIONS

The experimental data of Kinsey and Palm bear out these a priori expectations and reveal the complicated course of concentration change in the posterior chamber. The general validity of Equation (1) is strongly supported by the finding that with each of two different test substances—radioactive sodium and thiocyanate—Kinsey and Palm obtained an essentially identical estimate of the rate of aqueous flow, K_f . If we divide Equation (1) by $(C_p - C_a)$, we obtain

$$\frac{dC_a}{(C_p - C_a)dt} = K_f \frac{C_p - C_a}{C_p - C_a} + K_d. \quad (2)$$

This equation is evidently of the form

$$Y = K_f X + K_d.$$

Since X and Y can be determined from the experimental data, one test of the validity of Equation (1) is the linearity of a plot of X vs. Y .

Kinsey has supplied us with the experimental data to make this test possible. In order to be independent of previous efforts

TABLE 1
TURNOVER RATE OF SODIUM AND THIOCYANATE
IN RABBIT EYES

Time, Min.	SCN			Na		
	C_r	C_a	dC_a/dt	C_r	C_a	dC_a/dt
0	0	0	—	0	0	—
5	13	4	—	1	2	—
10	20	8	0.76	10	5	0.62
20	30	15	0.76	35	14	1.00
30	35	23	0.76	46	26	1.06
40	39	30	0.75	51	36	0.96
50	41	36	0.67	54	44	0.70
60	43	41	0.55	56	50	0.60
70	44	46	0.46	58	56	0.53
80	45	49	0.36	60	61	0.44
90	46	51	0.28	61	65	0.36
100	47	54	0.25	62	68	0.28
120	48	57	0.21	65	72	0.20
140	50	61	0.18	65	76	0.14
160	51	63	0.15	69	78	0.12
180	52	64	0.08	71	80	0.10
200	53	65	0.03	73	82	0.09
225	54	66	—	75	84	—
250	55	67	—	78	86	—
275	56	68	—	80	87	—
300	57	69	—	81	88	—
∞	61	74	—	99	98	—

at curve fitting, we have made our own estimates of the smoothed curves which seem best to fit the data. The results of this curve fitting are given in Table 1. Curves were drawn representing the course of the anterior chamber concentration with respect to time, and the slope of these curves at different time values was estimated graphically. The results are shown in the columns headed dC_a/dt in Table 1. C_p is arbitrarily assumed to be 100.

From the data of Table 1, values for X and Y have been computed:

$$X = \frac{C_r - C_a}{C_p - C_a} \quad Y = \frac{dC_a}{(C_p - C_a)dt} \quad (3)$$

The resulting plots are shown in Figure 1. In these plots data from the first 30 minutes of the experiments are omitted, since in the experiments a time lag of this order was required for the plasma levels of the test substance to be stabilized. Further discussion concerning the interpretation of data obtained early in the time course of these experiments will be given below. The application of this method of analysis to the data is less satisfactory in the case of

sodium than in that of thiocyanate. With sodium the steady-state concentration levels both for the anterior and for the posterior chamber are very nearly equal to the plasma concentration. Consequently, as the experiment progresses, the differences ($C_r - C_a$) and ($C_p - C_a$) both tend to become small, and the errors in their estimates percentually large. In spite of these difficulties, it will be seen that the data do fall reasonably well on straight lines for both substances. The slope of these lines gives estimates of the coefficient of flow K_f and have the value of 0.014 from the sodium data and 0.017 from the thiocyanate data. The mean value of 0.0155 would represent both sets of data within the experimental range of uncertainty.

The estimates compare well with the estimates reached by Kinsey and Palm⁴ through the application of numerical integration to their data. This is no wonder, since the two methods are similar ways for finding values of K_f and K_d to fit Equation (1) to the same experimental data. In the method of numerical integration arbitrary values of K_f and K_d are assumed for trial, and dC_a/dt is then calculated by applying Equation (1) to the experimental data. Using these estimates of the rate of change of the anterior chamber concentration for successive short time intervals, one reconstructs stepwise the time course of the anterior chamber concentration. Successive calculated curves are produced with successive test values of K_f and K_d , and those test values are chosen which yield a calculated curve in best agreement with the experimental data.

In the procedure which we have outlined dC_a/dt is estimated directly from the smoothed curve which fits the experimental data. Using this estimate in Equation (2) enables the selection of the "best value" of K_f and K_d by graphical procedures equivalent to least-squares calculations.

It will be seen, then, that the experimental results of Kinsey and Palm do, in

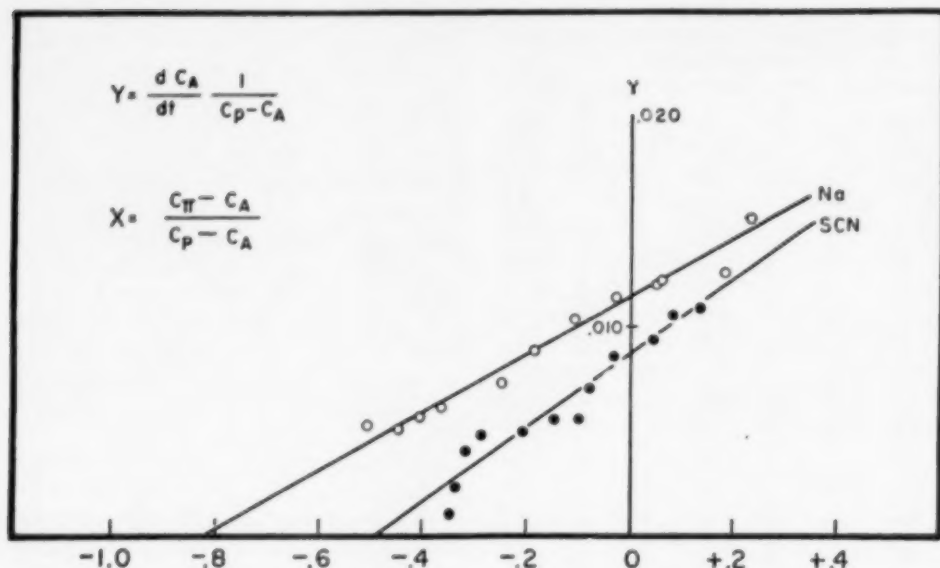


Fig. 1 (Friedenwald and Becker). Linear plot as a test of the validity of applying the Kinsey-Palm differential equation to their experimental data. The intercepts on the Y axis give estimates of K_4 ; the slopes of the lines give estimates of K_f .

fact, fit with reasonable approximation to Equation (1), but what are the assumptions that are made in saying that Equation (1) applies? The fact that Equation (1) fits does not prove that all other considerations are negligible. Now we shall attempt to analyze the quantitative role of some of the aspects omitted from consideration in formulating Equation (1). The assumptions involved in applying Equation (1) to the experimental data are (a) that the test substance is not metabolized within the eye; (b) that the posterior chamber provides a fair sample of fluid momentarily passing through the pupil; (c) that exchange of test substance between anterior chamber and cornea is negligible; (d) that outflow from the anterior chamber is in bulk, that is, without ultrafiltration; (e) that the posterior chamber tap provides a sample of fluid uncontaminated by anterior chamber aqueous or by vitreous, and (f) that no significant fluid volume enters the anterior chamber except via the pupil. The first of

these assumptions is obviously satisfied by the test substances which Kinsey and Palm used. Each of the remaining assumptions requires detailed analysis.

2. STREAMLINE FLOW THROUGH THE POSTERIOR CHAMBER

If there were perfect continuous mixing of the posterior chamber fluid, then a sample of this fluid would constitute an exact sample of the fluid momentarily passing through the pupil. The slow flow of fluid through the posterior chamber, however, precludes any appreciable mixing by turbulence. Thermal convection within the posterior chamber must be negligibly small. The elaborate baffles provided by the ciliary processes and by the zonule would seem to insure streamline flow. Under these circumstances the only appreciable mixing in the posterior chamber must be by diffusion from one streamline to the next.

If there is streamline flow through the posterior chamber, there should be a lag

period between the presentation of a test substance in the blood and its appearance in the pupil. During this lag period the test substance should be demonstrable in the posterior chamber. In experiments with Linnér, to be published elsewhere, this has been found to be true. With fluorescein as the test substance, a lag period of 60 to 80 seconds was observed with respect to appearance in the pupil, while at 20 to 30 seconds after intravenous injection the dye could be recovered in the posterior chamber.

The mathematical analysis of the problem is difficult, since the geometric form of the posterior chamber is very complex. One can approach the analysis by considering the posterior chamber successively (1) as a simple cylindrical tube, (2) as a right cylindrical annulus, (3) as an annulus the inflow surface of which is a cone such that streamlines from inlet to outlet are of varying length, (4) as an annulus of this form the inflow surface of which is corrugated, etc. For the first two hypotheses a full mathematical solution can be obtained. For the more complex hypotheses we have been able to reach only approximations. On the simplified Models (1) and (2), it is found that during the first few moments a mixed sample from the posterior chamber must give a very bad estimate of what is simultaneously passing through the pupil, but that after a time interval equal to five times the lag period the concentration in a mixed sample from the posterior chamber should differ from that simultaneously passing through the pupil by no more than four percent. The disparity becomes smaller the longer the experiment is continued.

To proceed from these simplified models to the complex structure of the actual posterior chamber involves the introduction into the model of variability in the lengths of streamlines, and of the complex intermingling of long and short streamlines. Variability in length of streamlines and the intermingling of long and short stream-

lines is a characteristic of turbulence. It seems likely, therefore, that actual events in the rabbit's posterior chamber will show less deviation from perfect mixing than is predicted on the basis of the simplified models. That this conclusion is at least partially true may be seen as follows:

Copeland and Kinsey⁷ have estimated the volume of the posterior chamber in rabbits as approximately one-fifth that of the anterior chamber. From some experiments to be reported elsewhere this would appear to be a slight underestimate, the true value being about one-third that of the anterior chamber. At any rate, the filling time for the posterior chamber, that is, the time required for the inflow of a volume equal to that of the posterior chamber, would be about 10-15 minutes. Now, on the basis of the simplified Models (1) and (2) given above, the lag period would be one-half or two-thirds the filling time. The actual lag period is only slightly more than one minute, indicating that some of the streamlines are short and swift, as in partial mixing.

It would seem appropriate to conclude that the posterior chamber samples early in the experiment are not fully representative of the fluid contemporaneously passing through the pupil. As the experiment progresses, errors from this source diminish. It was, in part, for this reason that in estimating K_f in the preceding section of this paper, data from Kinsey and Palm on experiments shorter than 30 minutes were omitted.*

It should be pointed out that when a sample of fluid is withdrawn from the posterior chamber, the valleys between the ciliary processes are not obliterated. Thus, the most recently secreted fluid lying, in part, in those valleys is not fully represented in the sample taken, and the sample

* In data to be published separately, it will be shown that under favorable conditions the linear relations expressed in Equation (2) are conformed to by data withdrawn as early as five minutes after the beginning of the experiment.

probably represents the fluid contemporaneously passing through the pupil somewhat better than would a theoretically correctly mixed sample.

3. THE CORNEA AS A RESERVOIR IN EXCHANGE WITH THE ANTERIOR CHAMBER

Equation (1) does not take into account any possible exchange between anterior chamber and cornea. If we wish to take account of such possible exchange, the equation must be rewritten

$$\frac{dC_a}{dt} = K_f(C_v - C_a) + K_d(C_p - C_a) + K_{dc}(C_c - C_a) \quad (4)$$

in which K_{dc} represents the diffusion coefficient for exchanges between anterior chamber and cornea (expressed in terms of anterior chamber concentration change) and C_c the concentration of the test substance within the cornea.

Maurice⁸ has reported experiments in which the concentration of isotopically labeled sodium in cornea, anterior chamber, and plasma was recorded following intravenous injection and other modes of administration of this test substance. From his data, $K_{dc}(C_c - C_a)$ can be estimated at appropriate time intervals. Equation (4) may be rewritten for comparison with Equation (2) as follows:

$$\frac{dC_a}{(C_p - C_a)dt} - K_{dc} \frac{C_c - C_a}{C_p - C_a} = K_f \frac{C_v - C_a}{C_p - C_a} + K_d \quad (5)$$

The right-hand side of Equation (5) is identical with the right-hand side of Equation (2). If we call the left-hand side of Equation (5) Y' , we may plot Y' vs. X just as we have previously plotted Y vs. X . As a matter of fact, Y' will differ from Y by a small correction, equal to

$$-K_{dc} \frac{C_c - C_a}{C_p - C_a}$$

Since C_a is, in general, larger than C_c , but smaller than C_p , this correction, in general, will be positive. Maurice estimates it to

be roughly 10 to 15 percent of Y . The net result of applying this correction is, therefore, to increase the estimate of K_f and K_d each by 10 to 15 percent. This would seem to be quite reasonable, since the volume of the cornea is about 25 percent of that of the anterior chamber and the 10 to 15 percent correction figure is equivalent to assuming that about one half of the corneal exchange of test substance is with the anterior chamber, and that the cornea achieves a final concentration comparable to that in the anterior chamber. Evidence that this is so, with respect to sodium, may be derived from Maurice's data.

Without the experimental determination of the time course of corneal concentrations of other test substances, the corresponding corrections cannot be computed. However, unless the final concentration in the cornea is higher than that in the anterior chamber, corrections larger than 10 to 15 percent are unlikely.

If we incorporate a 10 to 15 percent upward correction into the value of K_f , already estimated at 0.0155, we obtain an estimate of 0.017 to 0.018.

4. OUTFLOW IN BULK

An assumption underlying the formulation of Equation (1) is that, so far as it concerns the test substances to which this equation is applied, outflow is in bulk; that is, the concentration of the test substance in the efflux is the same as that momentarily present in the anterior chamber. The alternative possibility for consideration is that outflow might be by ultrafiltration, the concentration in the efflux being less than that in the chamber.

Ultrafiltration requires energy, and only 10 to 15 mm. Hg pressure is available to provide energy. For an ion, such as sodium, present in high concentration in the aqueous the available energy would not suffice to diminish the concentration in the efflux by as much as one percent. The outflow must, therefore, be substantially in bulk so far as concerns sodium. For other test sub-

stances the experimental concentrations used may be so low that this argument does not necessarily hold.

It is of interest to see how Equation (1) would be altered by assuming ultrafiltration to occur. Under such circumstances the outflow concentration would be nC_a , where n is some fraction less than unity.

$$\frac{dC_a}{dt} = K_f(C_p - nC_a) + K_d(C_p - C_a). \quad (6)$$

If Equation (6) is divided by $(C_p - C_a)$, we obtain

$$\frac{dC_a}{(C_p - C_a)dt} = K_f \frac{C_p - nC_a}{C_p - C_a} + K_d. \quad (7)$$

If the hypothesis of ultrafiltration at the outflow is correct, a plot of $dC_a/(C_p - C_a)dt$ versus $C_p - nC_a/C_p - C_a$ should fall on a straight line. We have already shown that for $n=1$ the plot is substantially linear. Our test, then, consists in finding whether other values of n yield plots which deviate significantly from linearity. It is readily found that with thiocyanate as test substance the hypothesis that n is 0.9 or less yields recognizably nonlinear plots. Consequently, outflow for this test substance is likewise substantially in bulk.

5. RELIABILITY OF THE POSTERIOR CHAMBER SAMPLE

Kinsey^{1,3} has discussed in considerable detail the question of the possible contamination of the posterior chamber samples by anterior chamber fluid. The evidence seems very good that such contaminations are avoidable in a properly performed posterior chamber tap. Contamination by vitreous fluid is less readily excluded. The insertion of the needle necessarily ruptures the anterior hyaloid and zonular boundaries. We have found that with sufficient patience appreciable volumes of fluid can be obtained directly from the vitreous cavity even with a fine needle. If, in attempting to obtain posterior chamber fluid, the tapping needle is twisted and turned,

very large samples of fluid may be withdrawn, samples several times as large as any reasonable estimate of the total volume of the posterior chamber. Such large samples, if taken early in the course of the experiment, contain concentrations of the test substance lower than those concurrently found in either chamber or plasma and comparable to those obtained by direct vitreous taps. It is, therefore, possible to contaminate the posterior chamber sample with vitreous. The chief safeguard against this is awareness of the hazard and care to enter the posterior chamber by a direct puncture, rotating the needle on its axis if necessary, but not shifting the axis during the whole procedure. At a later stage in our argument it will be possible to show that there is intrinsic evidence in the data of Kinsey and Palm making it unlikely that any significant vitreous contamination entered into their posterior chamber taps.

6. FLUID TRANSFER ACROSS THE IRIS

The aqueous is hypertonic with respect to plasma,² and the blood-aqueous barrier of the anterior chamber is permeable to water.⁹ It follows that some water must be transferred osmotically from plasma to anterior chamber. Equation (1) takes no account of this diluting procedure. The question is whether this effect is, in fact, negligibly small. At first sight, the osmotic water movement might be expected to be appreciable, for the permeability of biological boundaries to water in general exceeds their permeability to solutes, and, with respect to some solutes, diffusional exchange contributes an appreciable fraction of the anterior chamber turnover.

Kinsey has found that the posterior chamber aqueous is hypertonic with respect to anterior chamber aqueous by not more than one percent. It follows that the aqueous in its passage through the anterior chamber is diluted osmotically by not more than one percent. Any such dilution would consist, in part, in the diffusion outward of solutes and, in part, in the inward osmotic

transfer of water. The relative velocities of these two processes would be determined by the relative permeability of the barrier to water versus solutes, and this can be estimated only very roughly from the available data. However, even if all the dilution were water import, the net rate of osmotic inflow would be no more than one percent of the flow from posterior chamber, for the aqueous is diluted by no more than this factor in its passage through the anterior chamber. This is not to say that if one labeled the water molecules in the anterior chamber, one might not find them exchanging with plasma water at a very rapid rate. However, what we are concerned with here is not turnover rate but net transfer. The turnover rate of water is effected by the diffusional force of the total concentration of water, that is, some 55 osmoles per liter. The net osmotic transfer is effected by osmotic excess of aqueous versus plasma, that is, some 0.006 osmole per liter. The ratio of these forces is of the order of 10^4 .

This discussion can be put into more precise terms if we rewrite Equation (1) so as to include the osmotic dilution of anterior chamber aqueous

$$\frac{dC_a}{dt} = K_f(C_p - C_a) + K_d(C_p - C_a) - K_w C_a \quad (8)$$

in which K_w is the rate per minute at which the aqueous is being diluted. Since this rate can be no more than one percent of the rate of flow, and since the rate of flow, K_f , is approximately 0.017, it follows that a maximal estimate for K_w is roughly 0.0002. Kinsey and associates,⁹ using heavy water as test substance, found the turnover in the anterior chamber to be characterized by a rate coefficient of about 0.2 (half-life of three minutes). This is perhaps an underestimate of the turnover rate of water, since mixing in the anterior chamber might become a serious bottleneck under these conditions. The osmotic transfer is operated by a force 10^{-4} times

that operating the turnover. Hence a minimal estimate for the osmotic transport rate is 2×10^{-6} . The true value of K_w , therefore, lies between 2×10^{-2} and 2×10^{-4} . This small rate of dilution can be neglected with impunity in the analysis of aqueous humor dynamics.

Up to the present we have considered water transfer from iris vessels to anterior chamber by osmotic forces. The conclusion that the rate of such osmotic transfer is negligibly small would not, at first sight, appear to exclude simple hydrostatic ultrafiltration of fluid through the iris capillaries. The available pressure head for such ultrafiltration is the capillary blood pressure minus the intraocular pressure minus the protein osmotic pressure of the plasma. No exact estimate for this pressure head can be given, but it cannot be more than a few millimeters of mercury and may, in fact, be negative. When we compare this with the osmotic pressure excess of 100 mm. Hg, which we have already shown to be ineffective across this same boundary, we must conclude that under normal conditions the contribution of ultrafiltration from the iris capillaries is also negligible. With inflammation and other reactive changes in the iris vessels this would, of course, no longer be true.

PART II

1. POSTERIOR-CHAMBER DYNAMICS

In preceding sections it has been shown that the differential Equation (1) used by Kinsey and Palm for the analysis of their results is valid within rather wide limits and that the coefficients of flow and diffusion which they have calculated are reliable within the limits of accuracy of the experiment. It would be of great advantage if Equation (1) could be manipulated in such a way as to eliminate C_p (the posterior chamber concentration) so as to reveal what information, if any, can be obtained from knowledge of anterior chamber and plasma concentrations alone. All of the

older experiments present only data of this latter type, and, if we wish to compare these older data of this latter type, and if we wish to compare these older data with those including posterior chamber taps, a mathematical framework is required for such comparison.

The argument that follows is necessarily a complex one, and it may assist the reader to outline in advance the course it will take and why. What we want is an equation expressing the course of the concentration in the anterior chamber (C_a) as a function of time (t). Equation (1) tells us explicitly only about the rate of change of concentration in the anterior chamber. It is the differential equation whose integral we seek.

Equation (1) contains C_r as an independent variable, and before we can integrate Equation (1), we must obtain an expression for C_r as a function of time. To do this, we start by writing a differential Equation (9) for the posterior chamber which expresses our best intuitions as to how the test substance gets into and out of the posterior chamber. Since there must be diffusional exchange between posterior chamber and lens and vitreous, the concentrations in these structures enter as independent variables into Equation (9). For the sake of simplicity, we have lumped together vitreous and lens as if they constituted a single reservoir and have designated the concentration in that reservoir as C_r .

Just as Equation (1) cannot be solved without an explicit equation for C_r , so Equation (9) also cannot be solved without an explicit expression for C_r . Again, calling on our physiological intuition, we write a differential equation for the reservoir.⁸ Evidently, the reservoir must be in diffusional exchange only with plasma and posterior chamber. Equation (10), therefore, introduces no new independent variable. We have reached the end of writing new equations and can apply to the set (1), (9), and (10) standard mathematical

procedures leading to the solution we desire. We obtain, in fact, explicit equations for C_a , C_r , and C_r , each as a function of time. Each of these equations can, in turn, be compared with the experimental data. These equations are multiple exponential equations, and conventional graphical procedures are available to test their fit with the experimental data. In reaching these equations, it is convenient to introduce some new constants. It is, however, possible to define these new constants in terms of the diffusion and flow coefficients that are themselves defined in Equations (1), (9), and (10), plus the boundary conditions of the integration, which in this case are the initial and final (steady-state) concentrations in anterior chamber, posterior chamber, and reservoir.

All of this is done with the assumption that the plasma concentration remains constant during the experiment. Various other simplifying assumptions will be noted as the argument is developed. With this outline of the prospective argument in mind, we return to that argument in detail.

As noted above, Equation (1) contains C_r as an independent variable. In order to eliminate this variable, we start with an approximate differential equation for the posterior chamber.

Kinsey and Palm have suggested two forms for the posterior chamber differential equation, depending on whether the test substance enters by secretion (that is, at a fixed concentration relative to plasma) or by diffusion (that is, at a rate proportional to the concentration difference between plasma and posterior chamber). For the purpose of the present discussion these two equations will be fused into one.

$$\frac{dC_r}{dt} = K_{f_r}(C_s - C_r) + K_{d_p}(C_p - C_r) + K_{d_r}(C_r - C_s), \quad (9)$$

In this equation, K_{f_r} represents the rate of flow per minute as a fraction of posterior chamber volume; K_{d_p} , the diffusion co-

efficient between plasma and posterior chamber, and K_{d_p} the diffusion coefficient between the posterior chamber and the adjacent reservoir (vitreous and lens). If K_{d_p} is zero, this equation becomes essentially identical with the Kinsey-Palm secretion equation; if C_r is zero, it becomes identical with their diffusion equation. C_r is the concentration in the environmental reservoir. C_s may be defined as the concentration "secreted," or, more precisely, it is the concentration which would be reached in the posterior chamber at steady state if there were no diffusional gains or losses, i.e., if K_{d_p} and K_{d_p}' were zero.

Kinsey and Palm were fully aware of the simplifying assumptions involved in the formulation of their equations. The environmental reservoir, with which the posterior chamber is presumed to be in diffusional exchange, is, for purposes of simplification, assumed to be a single, well-mixed chamber characterized by a single-lumped diffusion coefficient. The posterior chamber itself is also assumed to be well mixed. The justification for the use of these simplifying assumptions by Kinsey and Palm and by us is that they make the mathematics manageable and that, as will be apparent later, they fit the experimental data with reasonable approximation.

In Equation (9), C_r , the concentration in the environmental reservoir, is an independent variable. Without any additional assumptions except that the reservoir is in diffusional exchange with both posterior chamber and plasma, one obtains a differential equation for the reservoir:

$$\frac{dC_r}{dt} = K_r'(C_s - C_r) + K_r''(C_p - C_r) \quad (10)$$

where K_r' and K_r'' are, respectively, the diffusion constants for exchanges between reservoir and posterior chamber and between reservoir and plasma, expressed in terms of reservoir concentrations.

In order to eliminate C_r and dC_r/dt from Equations (9) and (10), a third equation is

required. This is obtained by differentiating Equation (9) with respect to time, assuming C_p to be constant.*

$$\frac{d^2C_s}{dt^2} = K_{d_p}' \frac{dC_r}{dt} - (K_{f_p} + K_{d_p} + K_{d_p}') \frac{dC_s}{dt} \quad (11)$$

Eliminating C_r and dC_r/dt from Equations (9), (10), and (11) and writing K_s for $(K_{f_p} + K_{d_p} + K_{d_p}')$, and K_r for $(K_r' + K_r'')$, we obtain

$$\frac{d^2C_s}{dt^2} + (K_r + K_s) \frac{dC_s}{dt} + (K_r K_s - K_{d_p} K_r') C_s = \text{constant} \quad (12)$$

This equation is integrable and yields as its solution the double exponential

$$C_s = C_{s\infty} [1 - M e^{-K_1 t} - (1 - M) e^{-K_2 t}] \quad (13)$$

where $C_{s\infty}$ is the steady-state concentration in the posterior chamber.

$$K_1 = \frac{K_s + K_r}{2} + \frac{1}{2} \sqrt{(K_s - K_r)^2 + 4 K_{d_p}' K_r'} \quad (14)$$

$$K_2 = \frac{K_s + K_r}{2} - \frac{1}{2} \sqrt{(K_s - K_r)^2 + 4 K_{d_p}' K_r'}$$

M is a constant whose value can be determined by differentiating Equation (13) with respect to t and determining the rate of change of C_s at $t=0$.

$$\left[\frac{dC_s}{dt} \right]_{t=0} = C_{s\infty} [M K_1 + (1 - M) K_2] \quad (15)$$

From Equation (9) we have

* If C_p varies during the course of the experiment, C_s may also vary, possibly in simple proportion to C_p . If an explicit equation for the variation of C_p with time is available, the differential equations may still be integrable, but this will add greatly to the mathematical complexities without adding much to the information. For most substances, following a single intravenous injection, the plasma time course can be described by a single or multiple exponential equation. However, the graphical exponential analysis of the associated concentration course in the anterior and posterior chambers will not reveal these additional exponents unless they differ significantly in magnitude from those characteristic of experiments with constant plasma concentration.

$$\left[\frac{dC_r}{dt} \right]_{t=0} = K_{fs}C_s + K_{ds}C_p \quad (16)$$

Combining Equations (15) and (16) we obtain

$$M = \frac{K_{fs}C_s + K_{ds}C_p - K_r C_{r\infty}}{C_{r\infty}(K_1 - K_2)} \quad (17)$$

The steady-state value $C_{r\infty}$ can also be defined in terms of Equation (9). At the steady state the rate of change is zero, and we have

$$K_{fs}C_s + K_{ds}C_p + K_{dr}C_{r\infty} = K_r C_{r\infty} \quad (18)$$

Moreover, the steady-state value of the reservoir can be obtained in a similar way from Equation (10)

$$K_r' C_{r\infty} + K_r'' C_p = K_r C_{r\infty} \quad (19)$$

Thus, all the constants in Equation (13) are defined in terms of the constants in Equations (9) and (10). Moreover, Equation (18) makes it possible to evaluate C_s in terms of the diffusion and flow constants and the steady-state concentrations.

The two exponents K_1 and K_2 of the double exponential Equation (13) are defined by rather complicated Equations (14), which obscures their physical meaning. However, from Equation (14) it can be seen that if K_{ds}' and K_r' (both of which define the diffusional exchange between posterior chamber and reservoir) are sufficiently small, then $K_1 = K_r$ and $K_2 = K_r$. Thus, K_1 is approximately the turnover rate of the test substance in the posterior chamber, while K_2 is the turnover rate in the posterior reservoir. In order to define the latter more exactly, it will be convenient to obtain an equation for C_r in terms of t . This can be done by substituting Equation (13) and its first derivative with respect to time into Equation (9) and solving for C_r .

$$C_r = C_{r\infty} [1 - N e^{-K_1 t} - (1 - N) e^{-K_2 t}]^* \quad (20)$$

* Dr. Erik Palm points out that the exponents K_1 and K_2 occupy similar positions in the explicit equation for C_r , as they do in the equation for C_s .

where

$$C_{r\infty} = \frac{K_r C_{r\infty} - K_{fs} C_s - K_{ds} C_p}{K_{dr}'} \quad (21)$$

$$N = M \frac{(K_r - K_1) C_{r\infty}}{K_{dr}' C_{r\infty}}$$

In general, N turns out to be a small negative number, and K_1 contributes a small initial lag in the concentration time course of the reservoir. Thus, K_2 represents the filling rate of the reservoir after a small initial lag. Kinsey and Palm reached a similar conclusion in their less detailed analysis of the posterior chamber dynamics.

These equations do not invite too precise an interpretation, since in actual practice the reservoir-filling coefficient, K_2 , is a lumped coefficient representative of several chambers (vitreous and lens) and the experimental estimate of K_2 will be somewhat influenced by the segment of the semilog plot used for this estimation. Similarly, the experimental estimate of the turnover rate in the posterior chamber, K_1 , is blurred by the fact that no allowances have been made for the initial rapid rise of the plasma concentration. Nevertheless, our present purpose is precisely to determine whether or not these simplified equations do give an approximate description of the experimental events in the posterior chamber.

As the first step toward testing the empirical validity of Equation (13), we can inquire whether the posterior chamber data of Kinsey and Palm conform to this equation. Using the conventional method of graphical analysis, we have plotted $\log (C_{r\infty} - C_r)$ vs. t . The results are shown in Figures 2 and 3. Substantially good fits are obtained. The following values of the coefficients of Equation (13) for the two test substances studied may be tabulated.

It would appear that the values of K_2 are reasonably well established by this analysis. The estimates of K_1 are less cer-

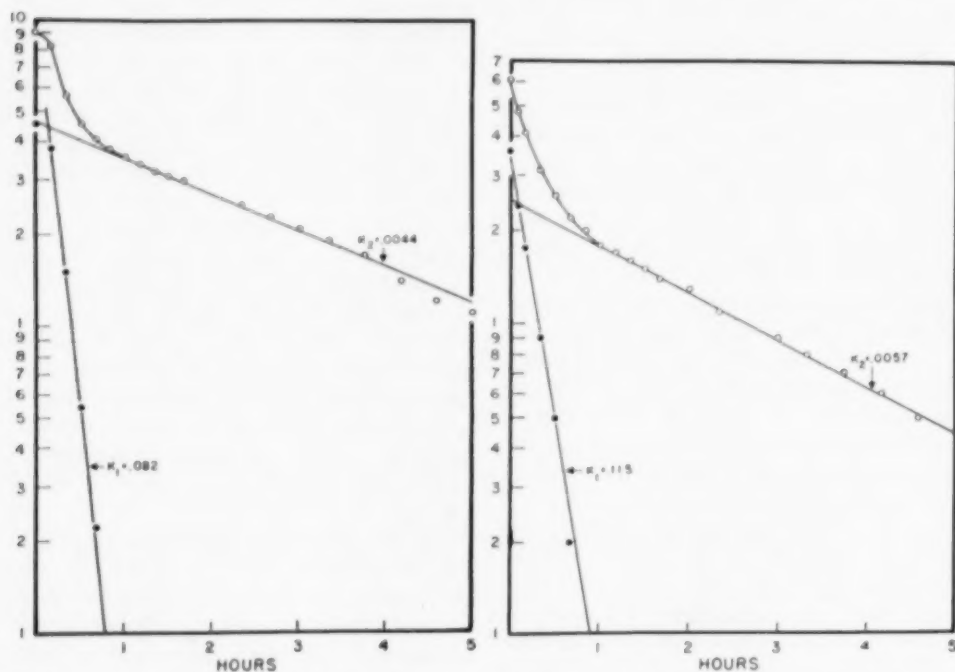
TABLE 2
VALUES OF COEFFICIENTS OF EQUATION (13) FOR
SODIUM AND THIOCYANATE

Test substance	M	K_1	K_2
Na^+	0.50	0.09	0.0044
Thiocyanate	0.57	0.115	0.0057

tain, since no allowance has been made in these calculations for the fact that the plasma concentrations are rapidly rising during the first 10–20 minutes of the experiment. In spite of this unresolved aspect of the problem, there is no question that the double exponential equation as formu-

lated (Equation 13) furnishes a very good empirical description of the course of concentration change in the posterior chamber.

In order to study this matter further, it has seemed desirable to obtain data concerning the concentration of at least one test substance in the vitreous. In a series of rabbits, 100 μc of radioactive Na^{24} as chloride in isotonic saline solution were injected intraperitoneally. Plasma, posterior chamber, anterior chamber, and vitreous samples were removed at chosen times. The samples were weighed, placed in small metal pillboxes previously mois-



(Fig. 2) Graphical exponential analysis of Kinsey and Palm's data for radioactive sodium in the posterior chamber. The open circles represent a plot of $\log (C_{\text{post}} - C_x)$ vs. time. A value of 0.92 is chosen for C_{post} , since this was the experimentally determined value at 24 hours after injection of the test dose. Using this figure omits consideration of an additional, very slow component, which is visible only in experiments lasting several days. A straight line is fitted to the tail of the open-circle data. The values indicated by this straight line in the early portions of the experiment are subtracted from the open-circle data, yielding the solid-circle data. The latter are satisfactorily fitted by another straight line, indicating that the experimental data conform approximately to a double exponential equation. The slopes of the two lines are measures of the two exponents K_1 and K_2 of such an exponential equation.

(Fig. 3) Graphical exponential analysis of Kinsey and Palm's data for thiocyanate in the posterior chamber. The treatment is the same as in Figure 2.

tened with a solution of detergent, made up to 1 cc. with distilled water, evaporated to dryness, and their activity counted, using a thin window counter. No correction for internal adsorption within the sample was found necessary. The anterior, posterior, and plasma samples showed a time course in relation to the experiment in essential agreement with the findings reported by Kinsey and Palm.

The vitreous samples were obtained with a No. 18-gauge needle inserted through the sclera at the equator and directed so that the point of the needle could easily be observed lying behind the posterior pole of the lens. Aspiration supplemented by moderate pressure on the sclera enabled the obtaining of taps 0.5 to 1.0 cc. in volume. From these large samples duplicate aliquots were used for counting. In view of the large volume, sufficiently high counts were obtained even on samples drawn as soon as 20 minutes after the intraperitoneal injection of the test solution. The radioactivity per gm. of vitreous fluid was recorded as percent of the simultaneously determined activity per gram of water in the plasma (95.4 percent of plasma weight). The data are shown in Figure 4, using 103 percent of plasma as an estimate of the steady-state value C_{∞} . Each point on the curve represents the average of four or more eyes. In all, samples were obtained from 33 eyes. The series was terminated with only this relatively small number of observations, because the agreement between paired observations was so good and the data plotted onto such a smooth curve that further experiments seemed unnecessary.

The time course of the concentrations found in the vitreous is well described by a single exponential with a small initial lag, as was to be expected from Equations (20) and (21). The exponent which characterizes the rate of filling of the vitreous is a good deal smaller ($K_v = 0.0015$) than that which describes the tail of the posterior chamber curve ($K_2 = 0.0044$). It should

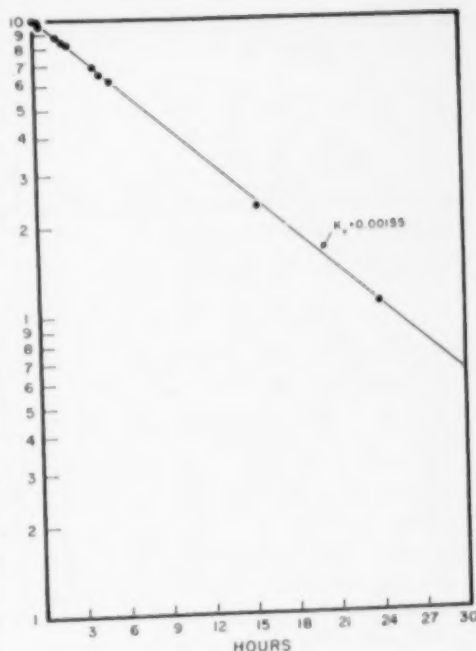


Fig. 4 (Friedenwald and Becker). Graphical exponential analysis of our data for radioactive sodium in the vitreous following a simple intraperitoneal injection of 100 mc. of Na^{24} as NaCl . The data conform to a single exponential equation after a small initial lag.

be remembered, however, that K_2 is the lumped exponent describing in one average figure the filling of the several compartments of the posterior reservoir. K_v , on the other hand, describes a single one of these compartments. Moreover, K_2 is determined experimentally mainly by the earlier part of the experiment and consequently represents, so to speak, the turnover rate of that part of the posterior reservoir that is closest to the posterior chamber.

2. ANTERIOR-CHAMBER DYNAMICS

The foregoing analysis has made it clear that the double exponential Equation (13) gives a fairly satisfactory representation of the course of concentration change in the posterior chamber. If we insert the value

of C_x given by Equation (13) into Equation (1), we have

$$\frac{dC_a}{dt} = K_f C_{ra} [1 - M e^{-K_1 t} - (1 - M) e^{-K_2 t}] + K_d C_p - (K_f + K_d) C_a \quad (22)$$

On integration, assuming C_p to be constant, we obtain

$$C_a = C_{a\infty} [1 + R e^{-K_1 t} - S e^{-K_2 t} - (1 + R - S) e^{-K_0 t}] \quad (23)$$

where $K_0 = K_d + K_f$ (K_0 is K_{out} in the earlier notation of Kinsey and others).

$$R = \frac{K_f C_{ra} M}{C_{a\infty} (K_1 - K_0)} \quad S = \frac{K_f C_{ra} (1 - M)}{C_{a\infty} (K_0 - K_2)} \quad (24)$$

The applicability of this equation to anterior chamber data may be tested by the usual graphic analysis. We wish to know the following: (1) Do the data conform to a triple exponential? (2) Do we obtain estimates of K_2 which agree with those obtained from the analysis of posterior chamber data? (3) Do we obtain an estimate of K_0 in agreement with our estimates of $K_f + K_d$ obtained from application of Equation (1) to both anterior and posterior chamber data taken together? We shall not expect exact agreement between the estimates of K_1 from anterior and posterior chamber data separately, since, owing to streamline flow in the posterior chamber, the concentrations found in the posterior chamber in the early parts of the experiment do not represent properly the concentrations in fluid simultaneously passing through the pupil.

Table 3 gives the comparisons of the relevant data.

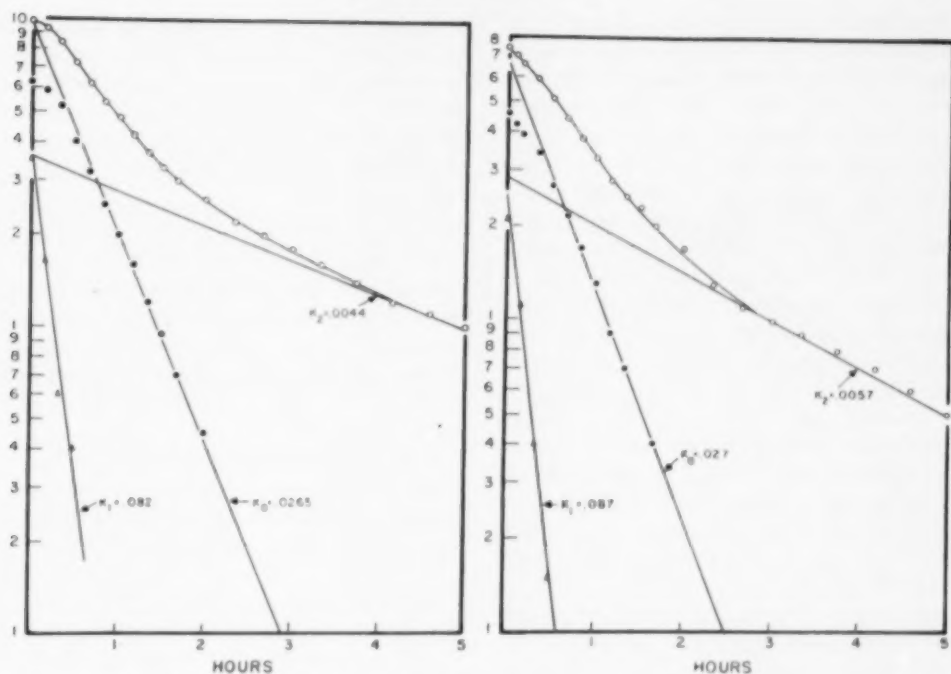
The graphical analysis of the anterior chamber data has been performed in two ways. In the first place, the anterior chamber data have been treated independent of similar graphical exponential analysis of the posterior chamber data. The results provide estimates of K_2 and K_0 given in Columns (2) of Table 3. It will be seen that the estimates of K_2 from the anterior chamber are in fair agreement with those from the posterior chamber, Column (1). Actually, the posterior chamber estimate of K_2 should be much more reliable, since the tail of the semilog plot of the posterior chamber data tends to be linear over a much longer portion of the experimental time interval (figs. 2 and 3). Consequently, we have redrawn the graphical analysis of the anterior chamber data using the posterior chamber estimate of K_2 for the tail (figs. 5 and 6). This gives the estimates of K_1 and K_0 shown in Columns (3) of Table 3.

The agreement of the estimates in Table 3 is remarkably good and makes it clear that approximate estimates of K_0 can be obtained by the exponential analysis of anterior chamber data through the application of Equation (23).^{*} Previous workers in this field have indeed attempted to estimate K_0 from anterior chamber data, but, because they were unaware of the large influence of the reservoir factor (K_2), serious underestimation of K_0 has resulted.

As an illustration of the effect of omitting consideration of the reservoir factor, the

TABLE 3
SUMMARY OF CONSTANTS FOR SODIUM AND THIOCYANATE

Test Substance	(1) Posterior Chamber		(2) Anterior Chamber		(3) Anterior Chamber Corrected		(4) Kinsey & Palm, K_0	(5) X vs. Y Plot, K_0
	K_1	K_2	K_2	K_0	K_1	K_0		
Na	0.09	0.0044	0.0033	0.031	0.08	0.027	0.030	0.026
SCN	0.115	0.0057	0.0054	0.026	0.09	0.027	0.027	0.026



Figs. 5 and 6 (Friedenwald and Becker). (Fig. 5) Graphical exponential analysis of Kinsey and Palm's data for radioactive sodium in the anterior chamber, showing that these data conform to a triple exponential equation.

(Fig. 6) Graphical exponential analysis of Kinsey and Palm's data for thiocyanate in the anterior chamber, showing that these data conform to a triple exponential equation.

thoughtful and extensive studies of Davson^{10,11} may be mentioned. Davson reports on experiments in which the plasma levels of a variety of test substances were kept constant for periods of two to three hours following the initial injections. Since the experiments were terminated after this relatively short period, true steady-state values for $C_{a,\infty}/C_p$ could not be obtained

directly. Davson applied graphical exponential analysis to the truncated data and estimated the steady-state concentration by finding out what value assigned to $C_{a,\infty}$ would render the tail of his exponential plot a straight line. He took the slope of this straight line as a basis for estimating K_0 . If we apply this method of analysis to Kinsey's data, we obtain for Na^+ and thiocyanate, respectively, 0.015 and 0.017 as estimates of K_0 , estimates which are 35 to 50 percent too low.

As a matter of fact, in Kinsey and Grant's original attack on aqueous humor dynamics, not only the reservoir factor but also the initial lag period (illustrated in Figures 5 and 6 by the upward convexity of the curve in the initial 10 to 20 minutes) was largely disregarded. In this early study a complicated graphical method was used

* The good agreement between the estimate of K_0 , from a consideration of the anterior chamber and plasma data alone, with the estimates of $K_f + K_d$, derived from application of Equation (1) to data, including those derived from the posterior chamber, enables us to give an answer to the question raised in Section 5 of Part I, above. In that section the possibility of contamination of the posterior sample with vitreous was noted. If there were a gross contamination of this sort, the inclusion of such data should lead to serious errors in the estimates. The good agreement of the estimates makes such contamination unlikely.

to estimate K_0 , in view of large statistical variations in the data. It is not easy to apply this method to Kinsey and Palm's present data, but that early method amounted in essence to an estimate of the K_0 on the assumption that a simple exponential equation was applicable to the data. On examining Figures 5 and 6, it is seen that the anterior chamber has reached half its steady-state value in 57 and 52 minutes, respectively. If a simple exponential equation were supposed to hold, this would lead to estimates of $K_0 = 0.012$ and 0.013 for Na^+ and SCN^- , respectively.

Kinsey and Grant, in their earlier study,⁸ assumed that K_f must be the same for all substrates and that for the substrate showing the smallest value of K_0 , K_d , the diffusional exchange between plasma and aqueous, was negligibly small. Thus, they reached an estimate of 0.010 to 0.012 for K_f . Though this earlier estimate is now shown to be too small, the achievement of this first approximation represented an important forward step at the time. As a matter of fact, the weight of the argument

in Kinsey and Grant's early publication was not on the validity of the first approximate estimate of K_f , but on the demonstration that an actual through-and-through flow of aqueous occurs, that is, the demonstration that K_f has some value greater than zero.

SUMMARY AND CONCLUSIONS

An analysis of the recent study by Kinsey and Palm⁴ shows that there are wide limits within which the differential equations, which they have used in the analysis of their data, may be considered approximately valid.

Accepting these differential equations as approximately valid, it is possible to construct a more general mathematical theory of aqueous humor dynamics than has heretofore been available. The application of this theory makes possible the resolution of a number of apparent contradictions in the literature on aqueous humor dynamics.

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CORNEOSCLERAL TREPHINING*

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Following corneoscleral trephining, when performed according to the technique originally described by Elliot in 1909, two unfavorable late complications—adhesion of the conjunctiva to the sclera or development of a large thin, cystic bleb—are likely to occur. The former may result in recurrence of the glaucoma from closure of the trephine opening by scar tissue; the latter may lead to hypotony from excessive filtration and may render the eye vulnerable to late intraocular infection.

In all subsequent modifications of Elliot's original technique, aimed at preventing these unfavorable developments, the variation has always been effected by a different rearrangement of Tenon's capsule. Elliot cut the capsule at its junction with the conjunctiva, but did not change its relationship to the sclera; Benedict separated it from the sclera and included it with the conjunctiva in his preparation of the flap; Verhoeff advanced it beyond the limbus on to the cornea; and Wilmer transplanted a detached portion of the area over the trephine opening.

It is the purpose of this paper to describe another modification in which the principle of advancing a fold of the capsule beneath the conjunctiva is employed (fig. 1).

Wolff¹ has described Tenon's capsule as a rather firm, inelastic membrane which covers the eyeball to within three mm. of the limbus, at which point it joins the bulbar conjunctiva. In front of the insertion of the rectus tendons it is separated from the overlying bulbar conjunctiva by loose areolar connective tissue, and between it and the underlying sclera is the loose episcleral tissue in the anterior portion of Tenon's space (fig. 2).

Schwalbe² believed that the inner surface

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Fig. 1 (MacLean). Diagram to show the relationship of the advanced fold of Tenon's capsule to the trephined area.

of the capsule and the opposing surface of the sclera were lined by endothelium. Benedict stated that the relation of Tenon's capsule to the sclera and the conjunctiva and the difference in elasticity of the capsule, sclera, and conjunctival tissue constitute the basis for the care needed to provide a satisfactory flap, one which will not impede the diffusion of aqueous humor through the conjunctival tissue.

It is generally believed that the potential

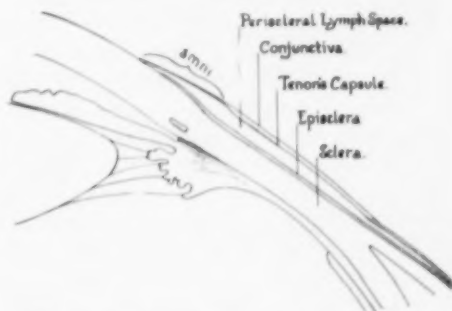


Fig. 2 (MacLean). Diagram to show the relationship of Tenon's capsule to the conjunctiva, sclera, and corneoscleral area.

drainage spaces are in the substantia propria of the conjunctiva between the conjunctival epithelium and Tenon's capsule and in the potential lymph space between the capsule and the sclera.

Two to three mm. behind the limbus, the conjunctiva, Tenon's capsule, and this sclera become rather firmly united. Forward from this line, only the conjunctiva covers the sclera and the limbus, and blends with the corneal epithelium one to two mm. anterior to the limbus (fig. 2). It is in this zone between the termination of Tenon's capsule and the termination of the epithelial layer of the conjunctiva, a zone about three mm. wide over the limbus, that the trephine opening should be made. From the trephine opening in this area the aqueous humor can diffuse beneath the conjunctival epithelium into loose areolar conjunctival tissue superficial to the capsule, and into the potential lymph space between the capsule and the sclera. It was stated by Benedict that most of the filtration occurs between the conjunctival epithelium and the capsule.

TECHNIQUE OF THE ORIGINAL ELLIOT OPERATION

In his first description of the operation, Elliot^{3, 4} advocated this formation of a large flap extending from the upper fornix to the limbus, including nearly a half of the anterior portion of the globe. The incision bounding the flap extended to the limbus on each side of the cornea, ending somewhat above the horizontal meridian. Later, in order to avoid cicatricial obstructions to the free flow of aqueous humor, he modified the flap by using a long curved incision beginning eight mm. from the limbus on one side and ending eight mm. from the limbus on the opposite side of the cornea in the horizontal meridian.

The incision was made in the conjunctiva only and the dissection in the plane between the conjunctiva and Tenon's capsule. To gain entrance to the sclera he incised the capsule at its junction with the under surface of the conjunctiva and from this point separated

the conjunctiva from the sclera and limbus to the cornea in the area chosen for the site of trephination.

Elliot used a two-mm. trephine in all of his operations. He later realized that such a large opening often resulted in undue exposure of the ciliary body and perichoroidal spaces. To overcome this and to permit a more anterior placement of the trephine opening, he later practiced splitting of the cornea for a distance of about 0.5 mm., using a sharp corneal dissector.

Following this operation, there usually developed either a small, localized, elevated, thinly covered, filtering bleb confined to the region just over the trephine opening, or else a flat conjunctival bleb with little or no filtration. When the bleb became elevated and thinly covered, it tended to override the limbus, encroach upon the cornea, and form vesicles which often ruptured and gave rise to attacks of intraocular inflammation. When the bleb was flat and adherent, filtration of aqueous was impeded and this often led to recurrence of the glaucoma.

In 1927, following a series of animal experiments on rabbits' eyes, Wilmer⁵ advocated the use of a Tenon's capsule graft to reinforce the conjunctiva and provide a thicker and more resistant type of bleb. In this operation a small portion of the capsule, four to six mm. in size, was placed under the conjunctiva in the region of the trephine opening. As this tissue was completely isolated from its blood supply, scar tissue developed and it became adherent to both the sclera and the conjunctiva. Although the immediate result was often good, the ultimate outcome was that filtration of aqueous was impeded and recurrence of the glaucoma often ensued.

In 1936 Verhoeff,⁶ realizing the vulnerability of such thinly covered blebs following trephine operations, described an overlying type of fornix-based flap, prepared by incising the conjunctiva at the limbus, in front of the trephine area, and undermining it for a distance of five to six mm. upward from the

limbus. To complete the operation, this flap, apparently comprising conjunctiva and capsule, was advanced over the trephine opening, beyond the limbus, and sutured to the barbed upper part of the cornea with one fine black silk suture.

This procedure obviously provided the trephine opening with a thick protective covering, but had the disadvantage of exposing it to infection by the close proximity of the conjunctival incision, and of reducing the filtering potential of the bleb by displacing forward the substantia propria of the conjunctiva. Other objections would be the cosmetic appearance and the danger of creating excessive corneal astigmatism.

It was believed by Benedict⁷ that the blebs which often followed the Elliot operation occurred as a result of adhesions between the conjunctiva and the sclera, caused by cutting Tenon's capsule in the area so close to the trephine opening. Accordingly, in 1940 he described a subcapsular approach for the preparation of the flap. Through a conjunctival incision 10 to 12 mm. above the limbus, the capsule is opened eight to nine mm. back of the cornea instead of at its anterior insertion, and the two structures, conjunctiva and capsule, are separated from the sclera to the line of firm union with the cornea just beyond the limbus. The bleb which followed this type of flap was usually broader, less elevated, and thicker, but as there was no tissue reinforcement of the conjunctiva immediately over the trephine opening, this area in many cases, particularly in elderly individuals where the conjunctiva and capsule are extremely thin to begin with, continued to be thinly covered and vulnerable to infection.

To meet many of the objections of these four types of flap, an attempt has been made to reinforce the conjunctiva by bringing forward a fold of Tenon's capsule and anchoring it under the conjunctiva by means of two laterally placed fine black silk sutures (fig. 1). In such a flap there is ample reinforcement of the conjunctiva, the substantia propria of the conjunctiva is not displaced, and

the smooth inner surface of the capsule and not the conjunctiva is brought to lie in apposition to the sclera in the filtering area.

TECHNIQUE OF MY OPERATION

Anesthesia is provided by the instillation of a 0.5-percent solution of pontocaine and by lid and retrobulbar injections of a two-percent solution of xylocaine. If general anesthesia is requested, pentothal sodium is preferable. If general anesthesia is used, it is always advantageous to inject locally with xylocaine also. Adequate fixation to control the globe is provided by one black silk suture in the superior rectus. The conjunctiva is grasped with delicate toothed forceps over the insertion of the superior rectus tendon, and with curved scissors a 12-mm. incision is made concentric with the limbus and 10 to 12 mm. from it (fig. 3). Through this incision Tenon's capsule, which is easily recognized, is grasped and incised with scissors just in front of the superior rectus tendon and in line with the incision in the conjunctiva (fig. 3). The anterior lip of the capsule is grasped and by blunt dissection is separated

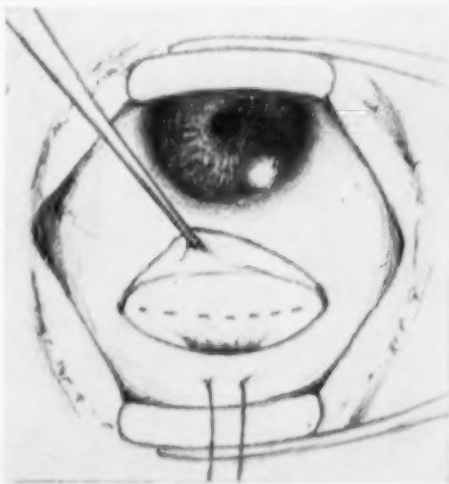


Fig. 3 (MacLean). Diagram to show the position and direction of the conjunctival incision which is made concentric with the limbus and 10 to 12 mm. above it. The broken line indicates the position of the incision in Tenon's capsule, which is made about eight mm. above the limbus.

from the sclera. To prevent adhesion formation later on, there should be no cauterization of any fine bleeding points in the episclera, particularly near the trephine area. For the same reason all dissection should be carried out with blunt instruments and a dull corneal dissector to avoid making any cuts in the sclera (fig. 3).

By gentle forward traction on the capsule with toothed forceps, the line of its firm attachment to the sclera is then opened, a dull corneal dissector—preferably a dull Took knife—being used, and by further dissection and gentle traction on the capsule the corneo-scleral junction is exposed over an area large enough to receive the trephine blade (fig. 4). At this time a shallow impression about three mm. in length may be made with a sharp Took knife held perpendicular to the corneal surface, just behind the conjunctiva at its junction with the cornea. This is done, not for the purpose of splitting the cornea, but merely to create a shelf for placement of the trephine blade, to prevent it from slipping forward and to prevent buttonholing of the conjunctiva.

The flap, comprising conjunctiva and cap-

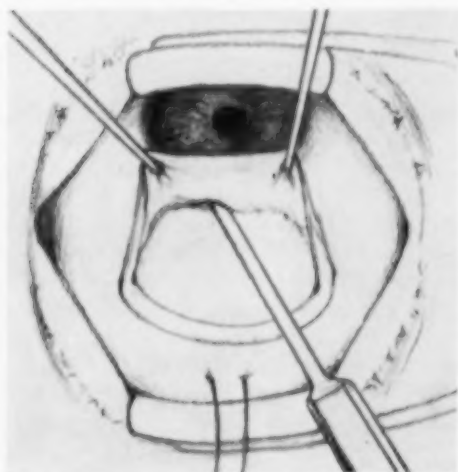


Fig. 4 (MacLean). The capsule has been separated from the sclera by blunt dissection. The conjunctiva is further separated from the central portion of the corneoscleral area to the cornea, a dull Took knife being used.

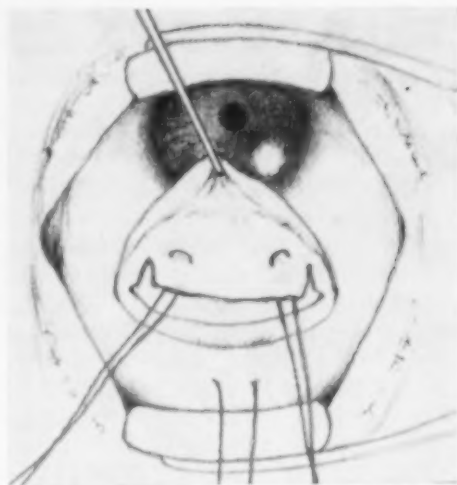


Fig. 5 (MacLean). Diagram to show placement of the anchoring sutures in Tenon's capsule. They are introduced from without inward, one on each side of the midline, eight to nine mm. apart, and five to six mm. from the cornea.

sule, is turned backward, and with the assistant grasping the lower cut edge of the capsule with toothed forceps and retracting it upward, and the operator grasping the conjunctiva with serrated forceps and retracting it forward, these two structures are separated by gentle traction and blunt dissection almost to their line of fusion (fig. 5).

Two 6-0 double-armed black silk sutures with atraumatic needles are placed in the capsule, from without inward, one on each side of the midline eight to nine mm. apart and about six mm. from the limbus (fig. 5). Both needles of each suture are carried superficially through the episclera close to the limbus, then out through the conjunctiva, opposite the 10-o'clock and 2-o'clock positions, and then laid aside to be tied later (fig. 6).

The flap is again turned down over the cornea, and by gentle traction on the capsule the site selected for the opening in the corneoscleral area is again exposed. The trephine blade is placed behind the ledge previously made at the corneconjunctival junction and with the handle held perpendicular to the surface a shallow impression is made

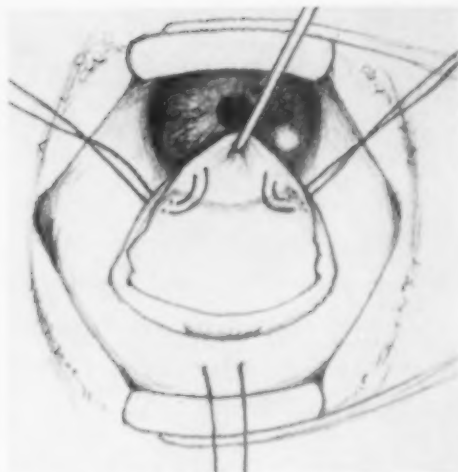


Fig. 6 (MacLean). Diagram to show the anchoring sutures being introduced through the episclera at the 10:30-o'clock and the 1:30-o'clock positions, and brought out through the conjunctiva on each side of the midline.

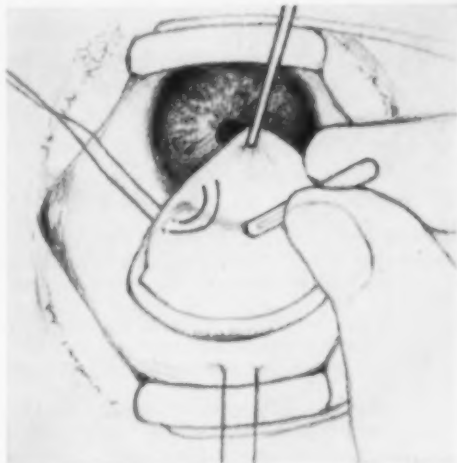


Fig. 7 (MacLean). Diagram to show placement of the trephine blade at the corneoscleral area immediately behind the junction of the conjunctiva and cornea in the midline.

part way through the scleral thickness. If, on inspection, placement is found to be correct, the handle is tilted forward about 20 degrees and rotated until penetration into the anterior chamber occurs at the lower or corneal margin (fig. 7).

The operator will sense this immediately because of a change in resistance to rotation of the blade, and because of slight movement of the pupil upward caused by the hinged scleral button turning upward and

the iris prolapsing into the trephine opening (fig. 8). Any attempt at complete cutting of the scleral button with the trephine blade at this time is unnecessary and undesirable and may result in damage to the zonules or ciliary body, or escape of the button into the anterior chamber (fig. 8).

When the trephine blade is removed, the portion of the iris immediately beneath this area will be seen bulging into the trephine opening, and the hinged disc of sclera, inner surface upward, will be seen lying on the

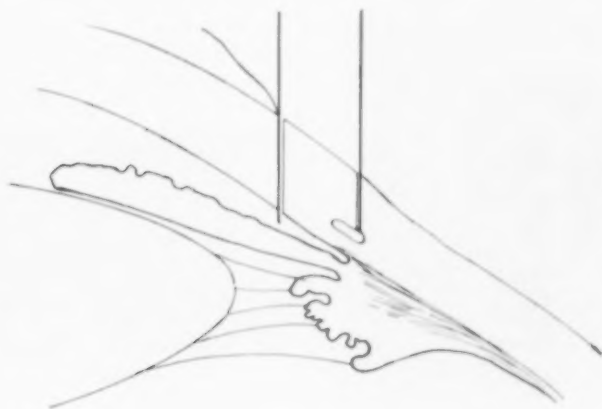


Fig. 8 (MacLean). Diagram to demonstrate how the button is cut completely through to the anterior chamber on the corneal side and a hinge is left on the scleral side by tilting the shaft of the trephine forward when the blade has penetrated halfway through.

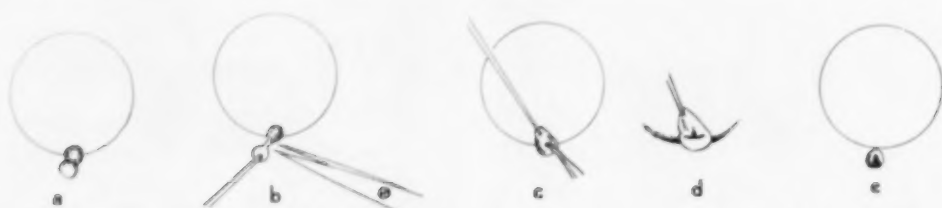


Fig. 9 (MacLean). (a) The button has hinged outward with the inner trabecular surface facing upward and the iris ballooned through the trephined opening.

(b) With slight traction on the button the inner portion (trabecular portion) is put on the stretch and can be cut without the point of the scissors entering the anterior chamber.

(c) A short meridional cut is made in the prolapsed iris concentric with the limbus close to the ciliary border but avoiding the ciliary body.

(d) One or two one-mm. radial cuts are made to enlarge the iridotomy or to do a small peripheral iridectomy.

(e) The appearance of the peripheral iridectomy, as seen through the trephined opening.

scleral surface just above the upper edge of the opening (fig. 9-a).

By gentle traction with narrow serrated forceps the inner attached portion—the trabecular portion—of the disc is put on the stretch and can be readily cut with delicate sharp pointed scissors, close to the margin of the opening, without entering the anterior chamber (fig. 9-b). The prolapsed iris is gently pressed forward and a short meridional cut is then made, concentric with the limbus and close to the ciliary border, but well away from the ciliary body (fig. 9-c). Two short one-mm. radial cuts are then made and a small portion of peripheral iris tissue removed (fig. 9-d and e).

The iridectomy should be just large enough so that the tip of the opening is just

visible through the margin of the cornea when the iris pillars have returned to the anterior chamber and the pupil has again resumed its normal size and shape (fig. 11).

Following completion of the peripheral iridectomy, the iris pillars usually return readily to the anterior chamber and the pupil reforms and contracts almost to its former size. This may be assisted by gentle stroking on the surface of the overlying conjunctiva with a smooth spatula at the limbus, just over the trephine opening (fig. 10). Seldom is it necessary to pass a smooth spatula through the trephine opening into the anterior chamber to replace the iris pillars.

The conjunctival incision is closed with one running 6-0 black silk suture (fig. 11). The preplaced capsule sutures are drawn

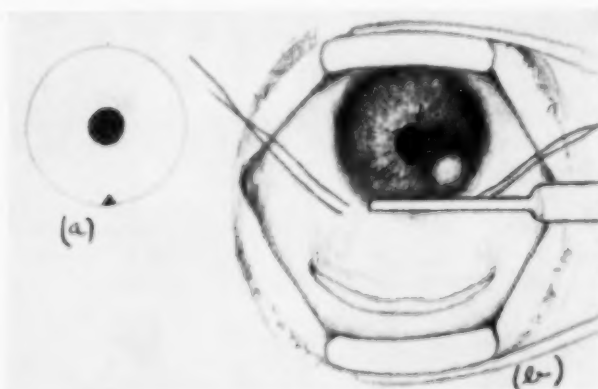


Fig. 10 (MacLean). (a) Appearance of the peripheral iridectomy as seen through the periphery of the cornea. (b) Replacing the iris by stroking on the surface of the conjunctiva over the trephined area and drawing the anchoring sutures forward to be tied.

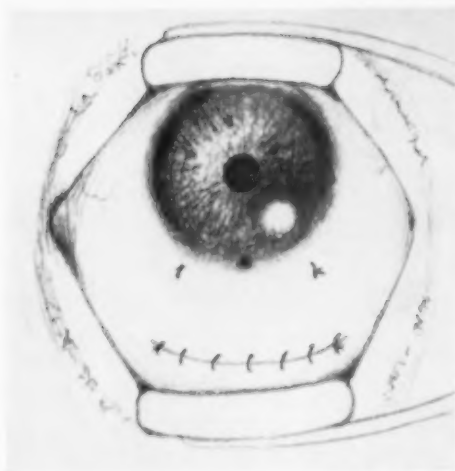


Fig. 11 (MacLean). Diagram to show the appearance of the eye after the operation has been completed.

forward and tied, and the folded capsule is assisted into position by gentle stroking with a smooth spatula on the surface of the overlying conjunctiva (fig. 11). The pupil should be kept small with pilocarpine for the first 24 hours, but atropine drops are used with each daily dressing from then on. All stitches are removed on the eighth or ninth day.

For the first few days the area of operation usually presents a smooth translucent, slightly raised, and slightly edematous appearance (fig. 12-a). In the course of a few weeks a fairly well delimited, slightly raised D-shaped or oblong area of filtration, five to six mm. in diameter, usually becomes established (fig. 12-b). The folded capsular tissue may be seen faintly through the semitranslu-

cent conjunctiva, like a spongy core about which aqueous seems to be filtering and diffusing laterally into the surrounding tissue. The conjunctiva never becomes tense, and seldom, if ever, does it overhang the limbus or encroach upon the cornea to any extent. The trephine opening is usually either completely obscured or only faintly visible (fig. 12-c).

The finger-driven Walker-Storz type of trephine, drilled out of solid tool steel and provided with two side windows and a smooth knurled handle, is safe, easy to operate, and preferable to other types for performing this operation. As it is always desirable to have the button hinged and not cut completely through by the blade, the battery-driven automatic trephine is unnecessary, and because it is so difficult for the operator to tell when the blade has penetrated to the anterior chamber with this type of trephine, it is more hazardous and less desirable. Only in the skilled hands of one accustomed to its use should this type of trephine be used. Spring-driven automatic trephines are no longer being manufactured and should not be used for this operation.

In trephining, the size of the fistula depends largely on the size of the trephine blade employed. Elliot used a two-mm. blade in all of his operations. Benedict pointed out the advantages of smaller sized blades. Recently 1.25, 1.0, and 0.75-mm. blades have been made available, and it is now possible to establish an opening varying from 2.0 mm. to 0.75 mm. in size (fig. 13). Because of the danger of damage to the ciliary body and

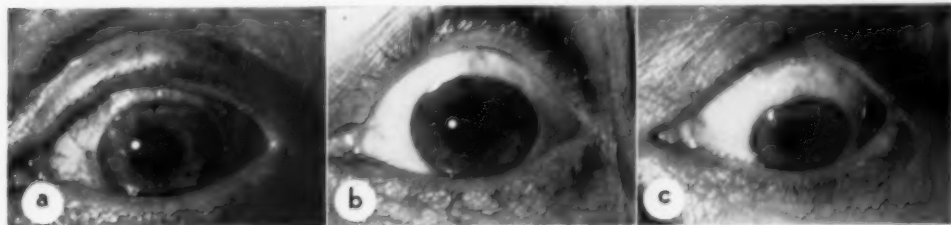


Fig. 12 (MacLean). (a) To show the usual appearance of the bleb about a week after operation. (b) The appearance about three weeks after operation. (c) The appearance several months after operation.



Fig. 13 (MacLean). Walker-Storz trephines (left to right): 2.0, 1.5, 1.25, 1.0, and 0.75 mm.

exposure of the perichoroidal spaces, unless corneal splitting is done, a 2.0-mm. blade should never be used.

If a fistula larger than 1.5 mm. is desired or if the anterior chamber angle is very shallow, or if the extension of the limbus on to the cornea is very narrow, an oblong opening, concentric with the limbus, can be established by making two overlapping 1.25-mm. impressions in the sclera. When one complete button has been removed the remaining portion of sclera outlined by the second impression can be readily grasped with straight iris forceps and easily cut out with sharp pointed scissors.

A 1.25-mm. opening provides adequate filtration for most cases of high base-pressure wide-angle glaucoma. A 1.0-mm. blade is more satisfactory in low base-pressure cases and a 0.75-mm. blade in the interim narrow-angle glaucoma.

INDICATIONS

1. *Wide-angle glaucoma.* It is generally agreed that corneoscleral trephining is more suitable for the chronic simple or noncongestive than for the congestive types of glaucoma; however, this operation may have to be resorted to in the latter if the tension remains uncontrolled after the acute congestive phase has been dealt with by iridectomy or some type of iris inclusion. In high base-pressure cases a 1.25 or 1.5-mm. trephine should be used, whereas in low base-pressure cases a 1.25 or 1.0-mm. trephine is not only

adequate but desirable. I still believe that trephining can be effective in wide-angle glaucoma in Negroes. Here, however, a larger, oblong, overlapping type of opening should be made.

2. *Narrow-angle glaucoma.* If there is any doubt that peripheral iridectomy or iridotomy will be successful in controlling the tension in patients with an acute or subacute type of narrow-angle glaucoma, trephining with a 1.00 or 0.75-mm. blade might prove more satisfactory than a linear incision at the limbus and might obviate the need for miotics later on. If there is difficulty in grasping the iris through an opening of this size, a fine sharp-pointed forceps should be used, or a short linear incision extending from the opening may be made with a knife and sharp-pointed scissors in a direction concentric with the limbus. This will close later, but a permanent small fistula would probably be established by the small trephine opening. Trephining is indicated in chronic narrow-angle glaucoma.

3. *Secondary glaucoma.* Trephining offers the safest, easiest, and most effective means of controlling the tension in glaucoma secondary to chronic uveitis.

4. *In aphakia,* trephining should be used only as a last resort, where cyclodialysis or other procedures have failed to control the tension.

5. *In chronic wide-angle glaucoma* associated with immature cataract, trephining may

be performed with the extraction in one procedure.

RESULTS

In 87 out of a total of 103 trephining operations performed in the six-year period from January, 1949, to December, 1954, a fold of Tenon's capsule was advanced to reinforce the conjunctival bleb. In the most recent cases sutures were employed in the manner described to anchor the fold; whereas in the earlier cases the capsule was simply pressed into position by manipulation with an iris reposer under and by gentle stroking over the conjunctiva.

Of the 87 operations in which capsular reinforcement was carried out, 81 were in wide-angle glaucoma, two in narrow-angle, and four in glaucoma secondary to active chronic granulomatous uveitis. There was complete normalization of the tension following 79, or 90.8 percent, of these operations. No patient in this series developed late infection.

In two of the six eyes in which there was a return of elevated tension following the initial operation, the operations were performed in the presence of active chronic granulomatous uveitis. In one eye there was essential atrophy of the iris with a large and poorly functioning pupil. One eye was in a Negro patient. In two eyes the cause could probably be attributed to episcleral trauma with resultant adhesions between the capsule and the sclera. In four of these eyes following a repeat operation, the outcome has been completely successful. In the remaining two the outcome has been fair, the tension being maintained at normal levels with the help of miotics.

In the cases with granulomatous iritis and in the colored patient a larger, more oblong opening should have been made at the first operation. In the eye with the essential iris atrophy a larger iridectomy should have been done. The pupil in this case failed to contract and free the iris from the edges of the trephine opening, with resultant closure almost immediately. A second operation with a

larger iridectomy performed within a comparatively few weeks has been completely successful.

The development of hypotony in both eyes of one patient could probably be attributed to the size of the trephine openings. The base pressure was low and the highest pressure never above 40 mm. Hg in either eye. A 1.0- or a 0.75- instead of a 1.50-mm. trephine should have been used and would have been adequate. Furthermore, preplaced sutures to hold the capsule in place were not used in this case and it was believed that some retraction of the capsule backward occurred. Following subsequent plastic operations, where a strip of Tenon's capsule was advanced and sutured to the episclera around the trephine area, there was return of the tension to normal in each eye.

Inclusion of the two cases with hypotony, later successfully corrected by separate operations, with those resulting in normal tension, would bring the figure for normalization of the tension by this operation to 93.1 percent. As the repeat operations resulted in complete normalization of the tension in four of the six eyes with recurrences, inclusion of these would bring the figure to 97.7 percent. In two of the repeat cases the outcome has been fair. At present the tension is being maintained at normal levels with the aid of miotics once or twice daily.

CONCLUSION

Two modifications of the corneoscleral trephining operation have been proposed:

1. Varying the size of the trephine opening to conform to the severity of the glaucoma.
2. Reinforcing the conjunctiva with an advanced fold of Tenon's capsule over the trephine area.

These should lessen the incidence of hypotony and late infection and make the operation a safe and satisfactory procedure not only for chronic simple wide-angle glaucoma but also for certain types of secondary and narrow-angle glaucoma.

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THE TOLERANCE OF HIGH TENSION IN GLAUCOMA*

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During the past two decades the experimental investigators have assiduously applied the techniques of physics and chemistry to ophthalmic problems, particularly to that baffling disease complex often called "chronic glaucoma simplex." The clinician has regarded this activity with some degree of awe and wonderment, realizing that if he was not cognizant of the new terminology and able partially to understand the concepts of tonography, facility of aqueous outflow, fluorometry, and so forth, he would be regarded as nonprogressive.

It is therefore with some hesitation and considerable temerity that I come to the habitat of the Dalai Lama of the experimental school and offer a mild query as to what extent our true understanding of this disease has been altered by this change of direction from the clinical to the experimental approach, and by the introduction of this new verbiage. This is particularly pertinent since another major Lama of this newer technique, residing in England, is beginning to wonder aloud where his activities are leading him.

It is my opinion that the clinician remains responsible for the treatment of the glau-

comatous eye and the preservation of its vision. He should therefore appropriate without shame all the pertinent data gleaned by the experimental investigators and ruthlessly discard many of their flights of fancy, always bearing in mind that the desired goal is a better understanding of the disease. This paper is an attempt to refocus the clinician's responsibility.

Despite the use of the word "glaucoma" since antiquity, it was not until 1830 that Mackenzie¹ gave a good description of the disease and mentioned elevated tension as a cardinal symptom. Following von Graefe's² demonstration of the lowering of intraocular pressure after iridectomy, the bulk of research and treatment of this disease has revolved around the concept of the raised tension, even though it was recognized that a progression of the disease could occur with a lowered tension.

In recent years the utilization of gonioscopic examination has accentuated the concept of the mechanical blockage of drainage as the chief factor in the production of this elevated pressure. There have been isolated objectors to this practically unanimous belief, but their objections have been overwhelmed by the amassed evidence of other observers. In spite of this near-unanimity of opinion, there are many factors that cannot be explained by elevation of tension alone

* From the Glaucoma Clinic of the Episcopal Eye, Ear, and Throat Hospital. Presented at the meeting of the Wilmer Institute Residents' Association, Baltimore, Maryland, April 1, 1955.

and by the relief of mechanical blockage. It is well known that vision was often lost when pressure was reduced surgically and the condition considered a surgical cure.

Duke-Elder³ is becoming increasingly dissatisfied with the modern concept of glaucoma, and is beginning to oppose this chamber angle and trabecular aspect of the disease. He is amassing heterogeneous evidence of the role of the vascular system in the regulation of intraocular pressure. He conceives the disease to be in its early stages an instability of vascular control, followed by a permanent and organic impairment of the capillary endothelium and sclerosis of the vessel wall. The first phase is associated with instability of tension, the second with its permanent elevation. The primary cause or causes of these vascular changes are at present quite unknown and much speculative writing has appeared in recent years on this subject, the greater part of which attributes the etiologic role to endocrine and humoral influences, or to a disturbance of the normal control by a vegetative center in the diencephalic region.

It is no secret that there is universal dissatisfaction with the treatment of glaucoma, which has been confined to the relief of a symptom rather than the primary disease.

Reese⁴ attempted to formulate a set of surgical rules dependent upon variations from base to peak pressure readings. He felt that the sustained elevation of the base pressure indicated a permanent damage to the filtration angle and that the higher this base pressure, the greater the drainage load the operation must carry. His working rule concerning the type of operation used both in shallow- and deep-angle glaucoma has not been adopted by other skilled surgeons.

Burke⁵ studied a series of satisfactory filtration operations which had been observed over five years and in which the tension had never been over 26 mm. Hg. In spite of this controlled pressure, there was further loss of visual field in about 50 percent of the cases.

Bloomfield⁶ has recently shown that in

cases of low-tension glaucoma where surgery was performed because of progressive loss of visual acuity and fields, there was no significant prevention of further deterioration.

Reese⁷ and Kronfeld and McGarry⁸ have demonstrated statistically that such operations are most successful early in the course of the disease, and that the results of surgery on eyes with advanced glaucomatous damage are generally poor.

Duke-Elder feels that the prognosis of simple glaucoma is on the whole not good, for even if the tension is adequately controlled, 30 percent of such cases do badly. Bloomfield and Kellerman⁹ investigated a series of eyes with advanced chronic simple glaucoma with uncontrolled tensions and concluded that central vision may be retained for long periods, but surgery merely hastened the visual loss in such cases.

All who have worked in large glaucoma clinics, particularly where Negroes form a considerable percentage of the patients, are well aware of the fact that enthusiastic surgery is not the answer to our glaucoma problem. We are often forced to advise operation because of the difficulty in making the patient understand the necessity of continuous miotic therapy and of repeated clinic visits at regular intervals. In other patients there is the problem of elevated tension despite repeated surgery, and further there is the one-eyed individual with the small visual field and continuously elevated tension. These problems are not answered simply, and in all clinics lead to frequent staff consultations and repetitious procrastination. It is as a result of this type of conference and thinking that the following study originated. The eight cases to be reported are all in Negroes with advanced chronic glaucoma of various types. The only common denominator is the elevated intraocular pressure over long periods of time. Some of these cases have had surgery, others not. The study is offered to indicate the length of time some eyes can tolerate such elevated pressures without going blind.

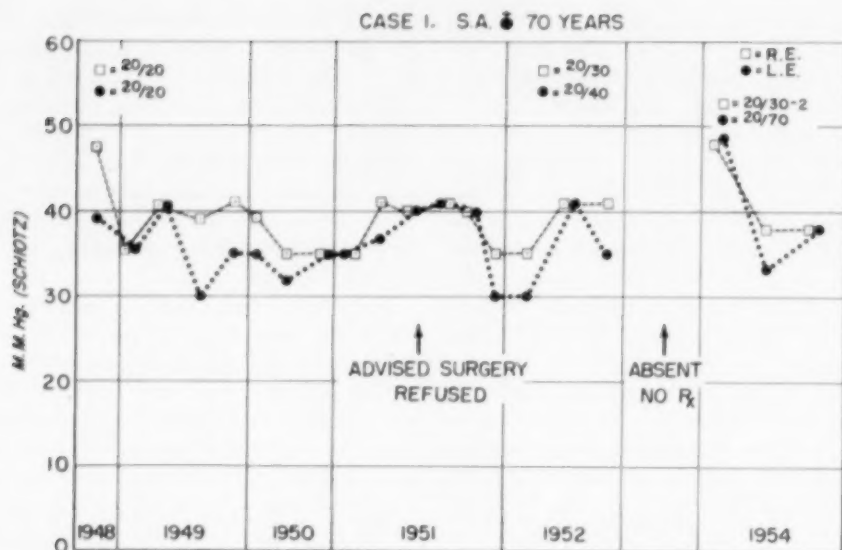


Fig. 1 (Rones). Chart for Case I.

CASE REPORTS

CASE I

S. A., a Negress, aged 70 years. The patient was first seen in the Glaucoma Clinic

in December, 1948, at which time the tension was right eye, 47.0 mm. Hg. and left eye, 39.0 mm. Hg (Schiotz). The vision was 20/20 in each eye. She was followed carefully and a variety of miotics was used; pilocarpine, eserine, furmethide, and fluoropryl. The tension over a period of six years was never recorded below 30, and was usually in the forties. In January, 1951, the corrected vision was 20/15 in the right eye and 20/20 in the left. In May, 1951, operation was advised but was refused, and she was continued on miotic therapy.

In spite of the elevated tension the vision in 1952 was 20/30 in the right eye and 20/40 in the left. She did not report to the clinic during 1953 and took no treatment. On her return in 1954 she still had 20/30-2 in the right and 20/70 in the left eye and a tension of 48.0 and 49.0 mm. Hg, respectively. There has been no loss in the visual fields. This patient has not returned to the clinic since 1954.

CASE 2

L. H., Negress, aged 66 years. She was

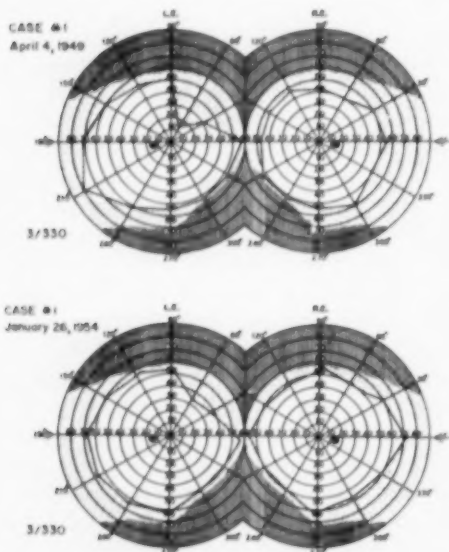


Fig. 2 (Rones). Visual fields for Case I.

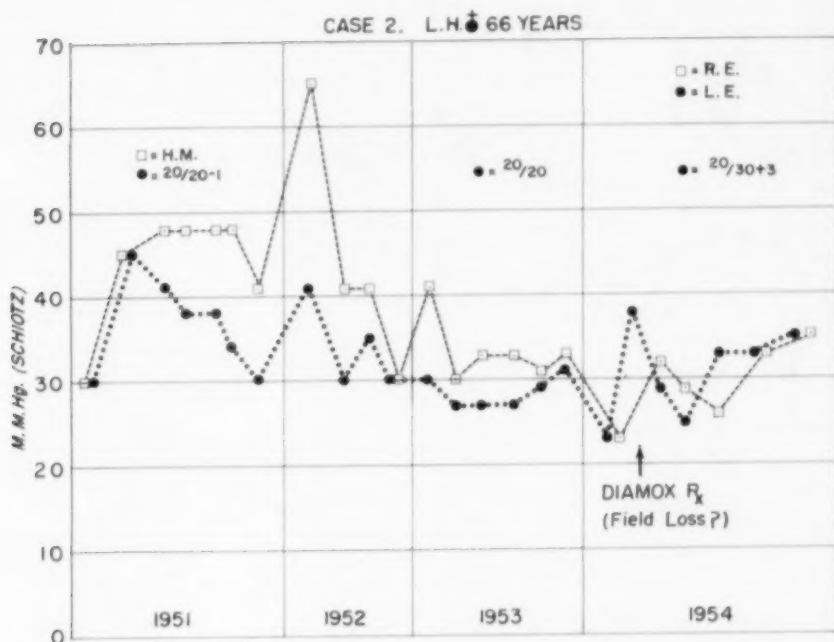


Fig. 3 (Rones), Chart for Case 2.

first seen in January, 1951, with advanced chronic glaucoma and the tension measuring 30.0 mm. Hg (Schiötz) in each eye. The vision was reduced to hand motion in the right eye but was corrected to 20/20 in the left. The visual field of the left eye was contracted, particularly in the upper nasal quadrant. She has been using a pilocarpine and eserine solution and the tension in her left eye has usually registered in the thirties, although on a number of visits it was recorded in the twenties.

In January, 1954, it was felt that she was losing some visual field and she was placed upon Diamox therapy but did not tolerate it well. The central vision continues good, and since this is her only functioning eye, it was felt that surgery was never indicated. On her last visit in February, 1955, the left eye maintained 20/20 vision, an unchanged visual field and a tension of 33.0 mm. Hg.

CASE 3

C. P., Negro, aged 50 years. He was first

seen in April, 1950, at which time the tension was found to be 41.0 mm. Hg in the right

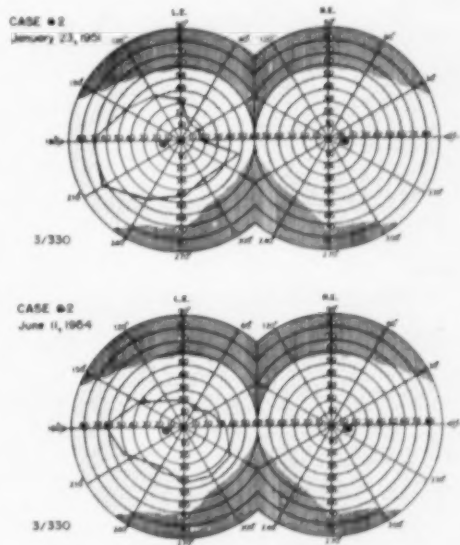


Fig. 4 (Rones). Visual fields for Case 2.

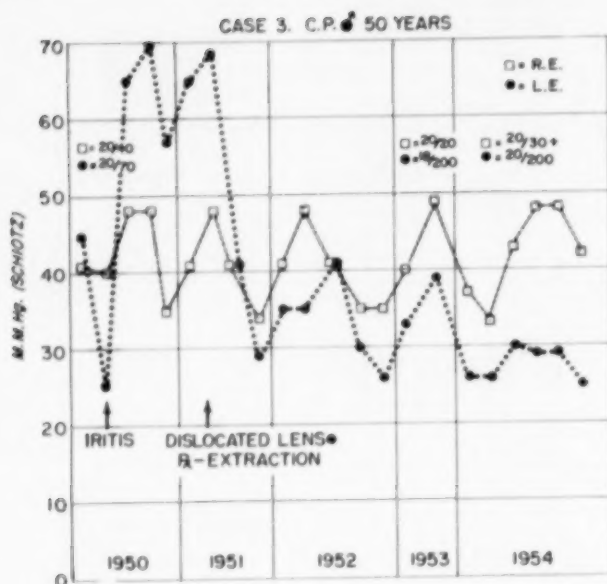


Fig. 5 (Rones). Chart for Case 3.

eye and 45.0 mm. Hg in the left (Schiötz). The discs appeared normal in each eye, but in the right eye, there were some perimacular scars of an old choroiditis. The vision

was corrected to 20/40 in the right eye and to 20/70 in the left.

In June, 1950, he developed an iritis in his left eye, and atropine was used, while continuing the use of pilocarpine in the right eye. The iritis cleared and the tension recorded 40.0 mm. Hg in the right and 25.0 in the left eye.

In August, 1950, he struck his left eye, with a resultant dislocation of the lens and a rise of pressure to 65.0 mm. Hg. The dislocated lens was removed surgically. A variety of miotics has been used in the subsequent course of treatment, and the tension in his left eye has been quite well controlled, but in the right eye it has remained persistently elevated. In February, 1955, the recorded vision was 20/30 in the right eye and 20/100 in the left eye, with a tension of 43.0 mm. Hg in the right eye and 27.0 mm. Hg in the left. The visual fields have remained virtually unchanged. It is felt by the staff that with the stability of vision and visual field, his only good eye should not be exposed to surgical risks in spite of the elevated tension.

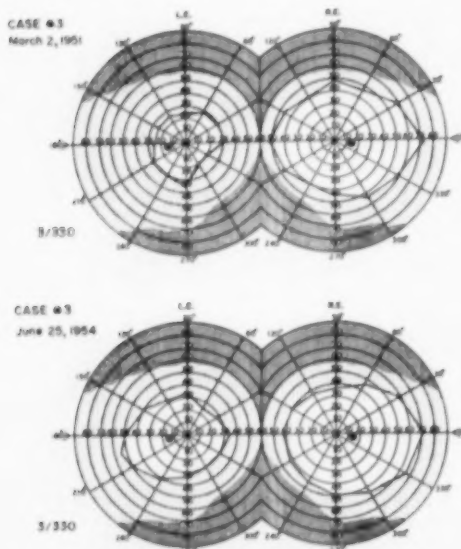
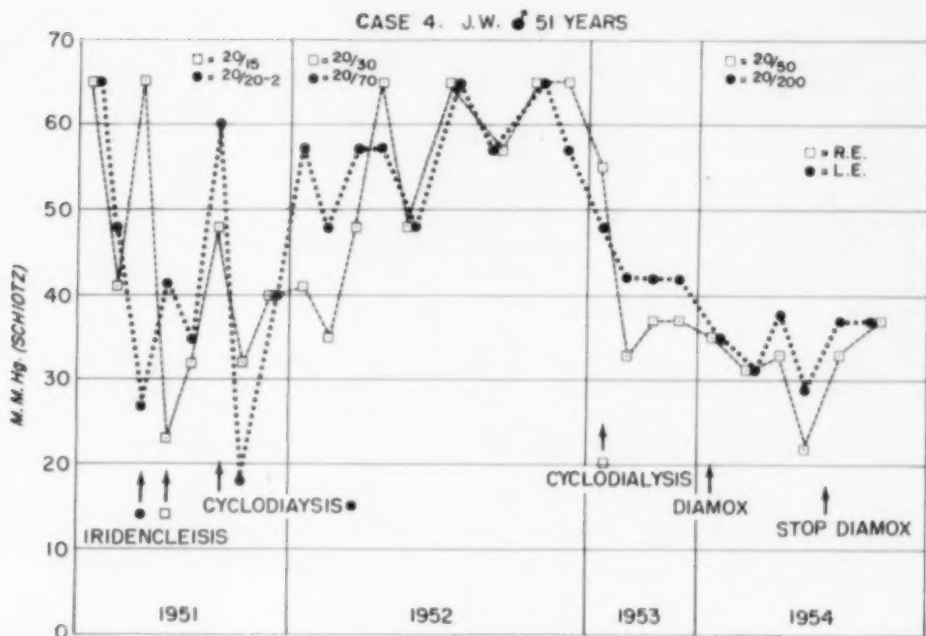


Fig. 6 (Rones). Visual fields for Case 3.



CASE 4

J. W., Negro, aged 51 years. The patient was first seen in January, 1951, with advanced chronic glaucoma, the tension being recorded as 65.0 mm. Hg (Schiotz) in each eye, and the vision corrected to 20/15 in the right and 20/20-2 in the left eye. Miotics did not lower the tension, so that an iridenceleisis was performed upon the left eye in February, 1951, and upon the right eye one month later. Within several months the tension in the left eye again became considerably elevated and a cyclodialysis was performed in October, 1951.

Following surgery, he has had local beta radiation therapy on one occasion and topical cortone therapy on another.

In April, 1953, a cyclodialysis was performed upon his right eye. In spite of this repeated surgery and the use of a variety of miotics and Diamox therapy, the tension has remained persistently and considerably ele-

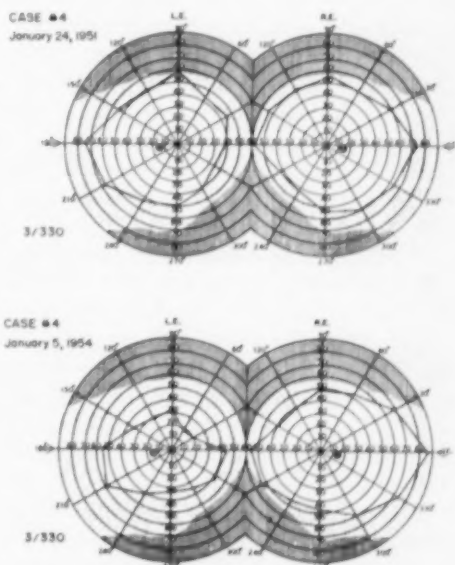


Fig. 8 (Rones). Visual fields for Case 4.

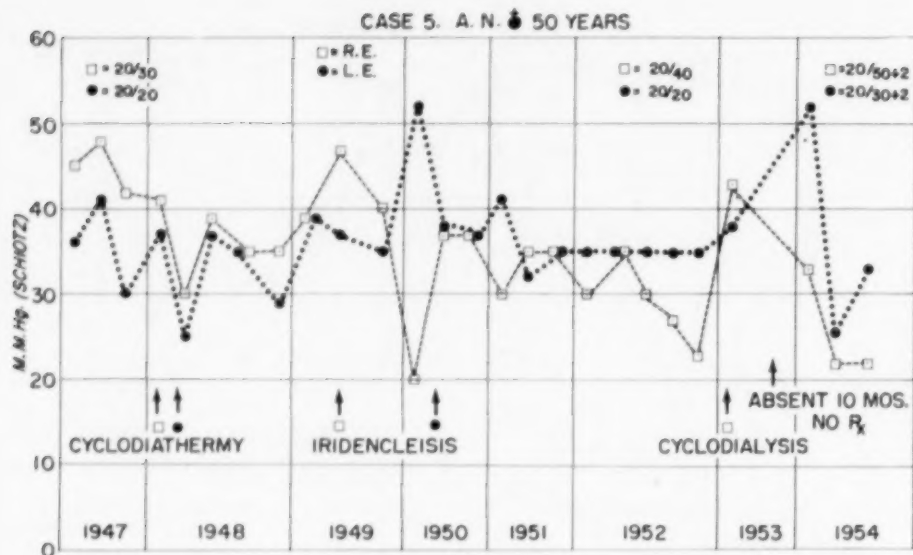


Fig. 9 (Rones). Chart for Case 5.

vated. The visual fields, however, have shown little change in his good eye and the vision in it is deteriorating only slowly, since in five years of elevated tension it has only decreased to 20/70 from the initial 20/15.

In March, 1955, the tension was 38.0 mm. Hg in the right and 43.0 mm. Hg in the left eye, with unchanged visual fields.

CASE 5

A. N., Negress, aged 50 years. Her first clinic visit was in March, 1947, at which time she was found to have an active uveitis with secondary glaucoma in the right eye and chronic glaucoma simplex in the left. The tension was 46.0 mm. Hg in the right eye and 37.0 mm. Hg in the left (Schiotz). Her physical survey was completely negative except for a positive blood Wassermann. The inflammatory reaction cleared and the right eye became quiescent, but the tension remained elevated in spite of therapy.

A cyclodiathermy operation was performed upon the right eye in January, 1948, and two weeks later a similar operation on the left eye. The tension still remained elevated

despite a variety of miotics. An iridencleisis was performed on the right eye in April, 1949, and in February, 1950, upon the left eye. During the next two years the tension remained persistently elevated.

In March, 1953, a cyclodialysis was performed upon the right eye. Following this she absented herself from the clinic for 10 months, during which time she had no treatment of any kind. On her return the tension was found to be 33.0 mm. Hg in the right and 52.0 mm. Hg in the left eye. She remained under observation for a few months and then moved away from the city.

What is the visual toll in this individual with repeated surgery and an elevated intraocular pressure of seven years' duration? In 1947, following the quiescence of the uveitis, the vision was corrected to 20/15 in each eye. In 1954, she still had a corrected vision of 20/50+2 in the right and 20/30+2 in the left eye. The visual fields showed slight constriction but no progressive loss. It is felt that this patient is maintaining her visual capacity quite well and that there should be no further surgery.

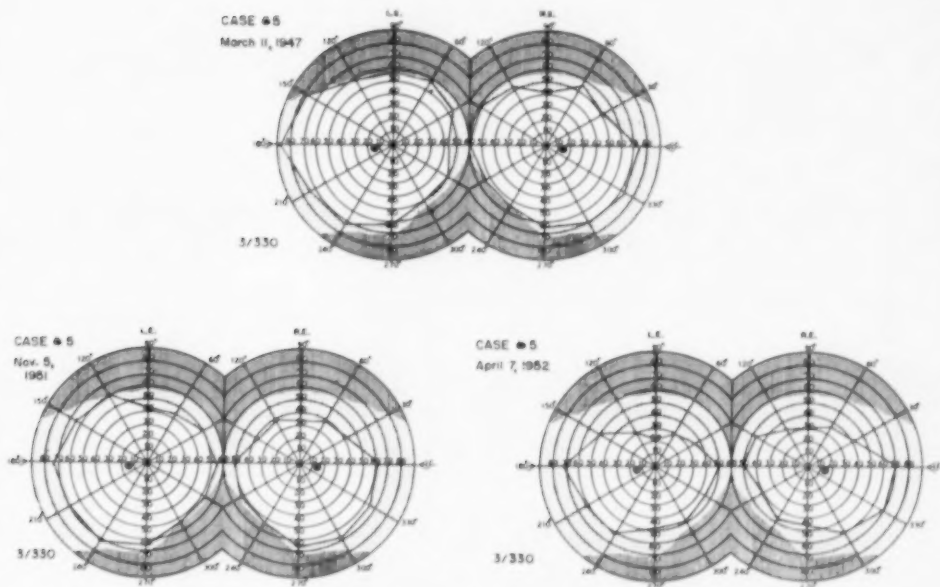


Fig. 10 (Rones). Visual fields for Case 5.

CASE 6

A. L., Negro, aged 50 years. He was first seen in December, 1943, with a history of a trephining operation upon his left eye 13 years previously. The left eye showed a chronic endophthalmitis with no light perception. The right eye was normal with 20/20—3 vision.

The inflammation persisted in the left eye so that it was enucleated in October, 1944. Pathologic examination of this eye showed sympathogenic uveitis, even though there was no clinical evidence of this disease in the right eye at the time of the operation. Two weeks after the enucleation, however, he developed an exudative iridocyclitis in his right eye, with many posterior synechias and corneal deposits, and a reduction of vision to 20/50. Under local therapy the eye became quiescent and upon discharge from the hospital the vision was 20/100 and the tension 30.0 mm. Hg.

During 1945, he was seen on numerous occasions with considerable discussion among

the staff members as to the validity of miotic or mydriatic therapy. Both were tried, but the tension remained elevated and surgery was advised but refused by the patient. It was noted on numerous occasions that the disc was of good color with no exaggerated cupping. In 1949, the patient stopped all treatment and the case was closed in this hospital.

He did not reappear at the Glaucoma Clinic until June, 1951, and during his absence he had been under no form of treatment. The vision was 20/30 and the tension 41.0. He was again put upon miotics and during the next two years the tension was never recorded below 35.0 mm. Hg. Surgery was again advised and again refused by the patient.

Once more he absented himself from the clinic and did not reappear for one year. On his last visit in March, 1955, the vision in the right eye was 20/50 and the tension 43.0 mm. Hg. The visual field has become slightly more contracted.

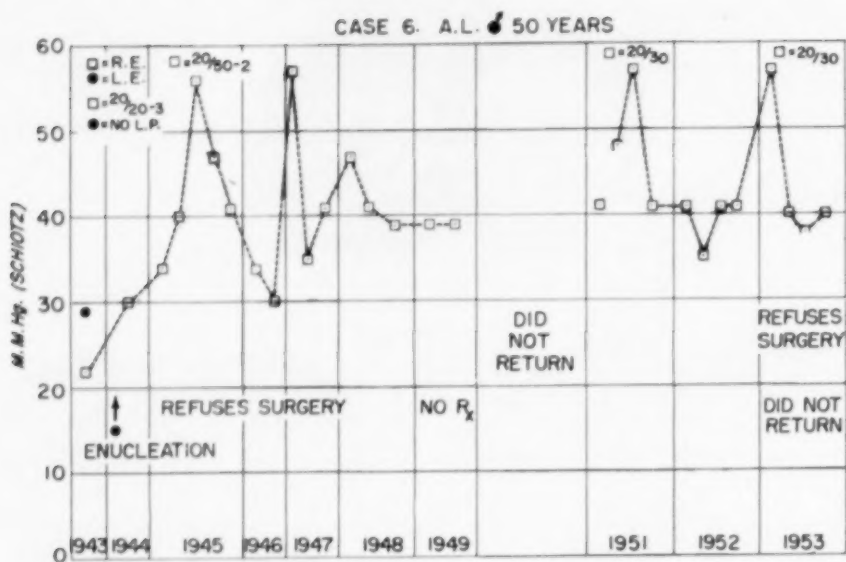


Fig. 11 (Rones). Chart for Case 6.

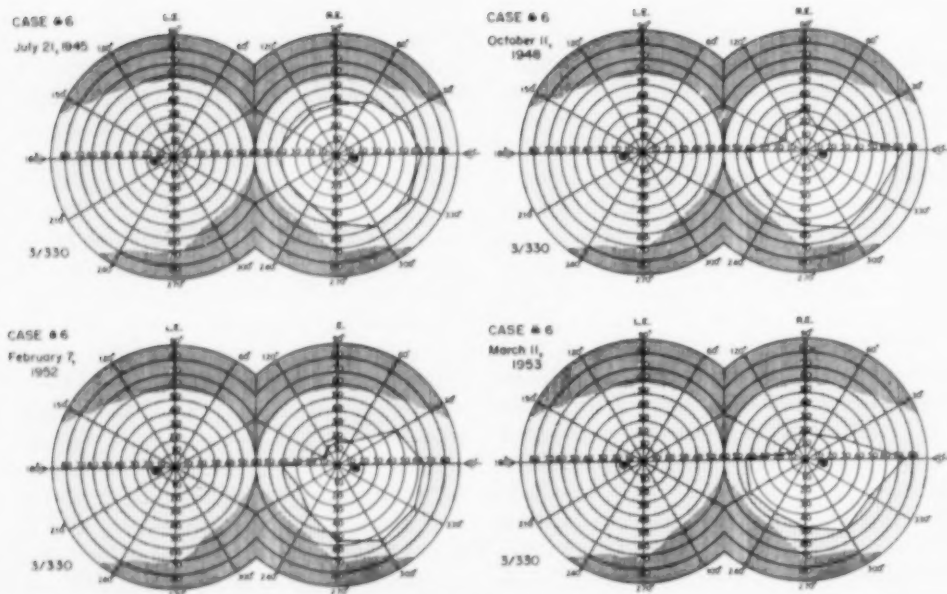


Fig. 12 (Rones). Visual fields for Case 6.

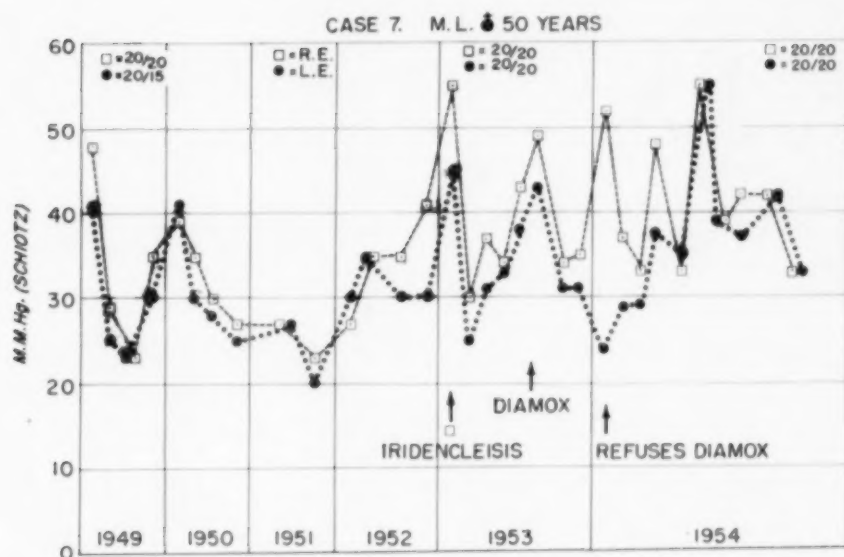


Fig. 13 (Rones). Chart for Case 7.

CASE 7

M. L., Negress, aged 50 years. She was first seen in the Glaucoma Clinic in June, 1949, at which time the vision was 20/20 in the right and 20/15 in the left eye, the discs were normal but the tension was 48.0 mm. Hg in the right eye and 41.0 mm. Hg in the left (Schiotz). The diagnosis was chronic glaucoma simplex and she was placed upon miotic therapy.

On several occasions during the next four years, her tension was recorded within normal limits, but usually it was elevated. In October, 1953, an iridencleisis was performed upon the right eye. The tension still remained elevated so that she was given Diamox but refused to take it because of the nausea and diuresis it induced.

A wide variety of miotics has been employed but the tension remains elevated. However, the vision is maintained at 20/20 in each eye, and there has been no definite loss of the visual fields, so that a policy of "watchful waiting" is being pursued. In

March, 1955, the vision is 20/20 in the right and 20/15 in the left eye, with a tension of 37.5 and 29.0 mm. Hg, respectively.

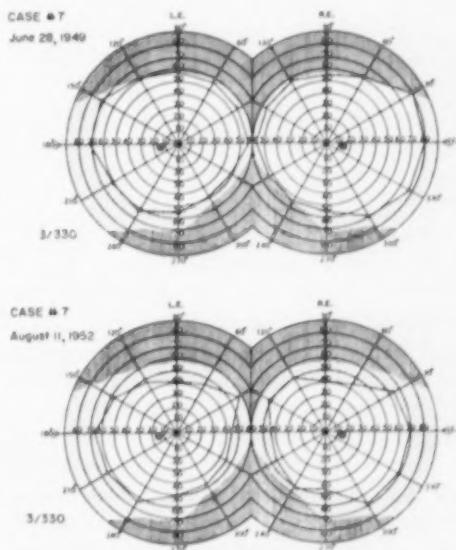


Fig. 14 (Rones). Visual fields for Case 7.

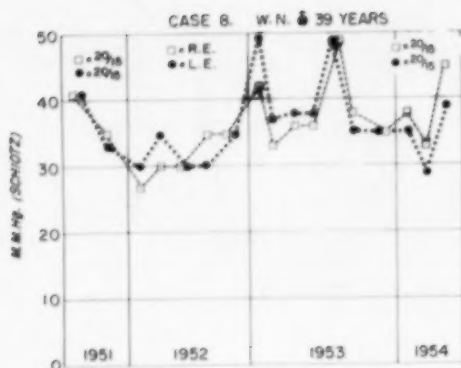


Fig. 15 (Rones). Chart for Case 8.

CASE 8

W. N., Negress, aged 39 years. She was first seen in the Glaucoma Clinic in October, 1951, with vision of 20/15 and tension of 41.0 mm. Hg (Schiotz) in each eye. The diagnosis was chronic glaucoma simplex and she was placed upon miotic therapy. The tension has remained elevated during the past three years but the vision remains 20/15 in each eye and on only one occasion was there thought to be any loss in the peripheral visual field. Surgery has been deferred because of the maintenance of visual function in spite of the elevated tension.

Her last visit was in March, 1955, when she had vision of 20/15 and a tension of 48.0 mm. Hg in each eye, with no loss in the visual fields.

DISCUSSION

These eight cases are offered not to chart a course for the treatment of glaucoma, but rather to induce greater doubt in our minds that the modern concept of glaucoma therapy is the only true one, and that any deviation from orthodoxy in treatment is fraught with danger to the patient.

The intraocular pressure has remained elevated in these eight patients over a long period of time for a variety of reasons. In spite of this, the visual capacity of the eyes has remained fairly good and entirely consistent with the aims of the Glaucoma Clinic. When measured with the results of glaucoma

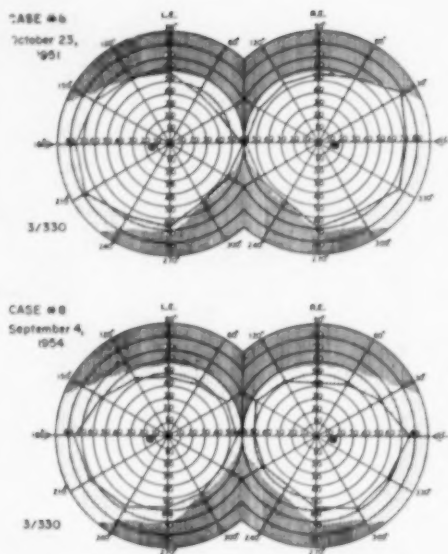


Fig. 16 (Rones). Visual fields for Case 8.

therapy in private patients, the comparison is not unfavorable.

It is not my conclusion that we should abandon our attempts to reduce the tension whenever possible, nor do I wish to infer that there is any beneficial effect from a prolonged elevation of the pressure. However, it is obvious from this series that some eyes can tolerate such elevations of pressure over prolonged periods of time, and that it is the duty of the mature clinician to evaluate all the factors involved, of which tension is only one aspect.

There should be no panicky resort to surgery merely because the pressure readings of an instrument are above a certain level, nor should surgery be indulged in by the enthusiast who believes that an operation should be performed as soon as the diagnosis of glaucoma is made to "prevent" further deterioration. The decisions required of the clinician in the proper handling of glaucoma are just those that are cultivated by years of observation and contemplation and cannot be replaced by any of the newer tests or techniques that have come into use.

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EYE-BANK PROGRAM

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The primary purpose of any eye-bank program is to make available to surgeons trained in keratoplasty a supply of usable graft tissue. Keratoplasty, the replacement of cloudy corneal tissue with clear cornea from a human donor, has a primarily optical purpose, though grafts are also done for tectonic and therapeutic reasons.

The major source of donor tissue in the United States is the Eye-Bank for Sight Restoration, Inc., a nonprofit agency founded in New York in 1945. The eye-bank collects and allocates donated eyes on a nationwide basis, implementing its program through its regional banks, affiliated hospitals, and the air lines and Red Cross Motor Corps, which provide free transport services.

The eye-bank program, like those developed more recently in several other countries, was initiated to expand the supply of donor material for keratoplasty and to transport this perishable tissue quickly to eye surgeons in need of it. Historically, it grew out of the demonstration by Filatov,² in the 1930's that corneal tissue from preserved cadaver eyes was as usable for corneal transplantation as that from eyes excised from living people because of ocular pathology. Filatov's finding meant that keratoplasty could be greatly expanded, provided surgeons could gain access to cadaver tissue. Knowl-

edge was growing as to which types of corneal pathology lent themselves to corneal grafting, and surgical techniques were being refined.

In the United States, however, as in many other countries, the matter of obtaining donor tissue was complicated by legal restrictions as well as personal prejudice. Under the law in the 48 states and the District of Columbia, the right of possession in a dead body is vested in the nearest surviving family, whose permission must be obtained prior to enucleation. The eye-bank, which functions through persuasion and the enlistment of voluntary services, has directed its educational program toward persuading people to donate their eyes after death because such a wish, in writing, usually has a binding moral effect on the surviving family.

The optimum method of providing donor tissue varies, of course, from country to country, depending on the legal structure, the feasibility of its change, the pattern of medical services, the location of hospitals, and of surgeons trained in keratoplasty.

In Britain, eye-banks are being developed at regional centers where surgeons trained in keratoplasty will be available.⁶ This plan implements a 1952 law authorizing prompt enucleation of eyes after death if neither the deceased during life nor the surviving family

have expressed objection to this procedure. Donor tissue is supplied in Holland, as in the United States, through a voluntary program functioning within the existing legal framework of the country.¹ The Netherlands Red Cross conducts a publicity program aimed at persuading relatives of the dead to permit enucleation for keratoplastic purposes. In Argentina, which has two eye-banks, desperately ill patients in hospitals are asked to donate their eyes after death.⁶ Donor tissue continues, however, in short supply.

In some countries, as Switzerland,³ donor material is obtained through a sort of tacit agreement to sidestep legal technicalities. In others, such as India,⁷ where the need for keratoplasty is great, severe obstacles remain.

These varying patterns reflect, of course, national differences. A co-ordinated national service offers several advantages for the United States. Donor material is available only by consent. A broad educational program conducted by a single agency affords the best public response.

Since the maximum length of time donor tissue can be preserved is three days, an efficient cross-country transportation system is essential. A single program can best enlist the voluntary services of transportation agencies. Fund-raising also can be most effectively done by a single service. Duplicate facilities and competing appeals are self-defeating.

The country is large and has many scattered and isolated hospitals. A unified service affords the best means of giving all qualified surgeons access to donor tissue. The eye-bank now has seven regional banks functioning within its aegis. The regional unit, like the New York bank, serves as a clearing-house, transferring tissue surplus at one institution to the eye surgeon in need of it, wherever he may be. To promote close liaison between the various bank units, a national co-ordinating committee representative of all the banks has been organized.

A single nationwide program can also serve as a brake on poorly organized or superfluous bank projects. Any eye-bank is

necessarily a major undertaking. It requires thoughtful planning and sound financial support. An eye surgeon trained in keratoplasty must supervise every aspect of its work. He must, for example, judge the usability of each donor eye, basing his evaluation on the accompanying history, as well as the actual condition of the cornea. Each eye must be cultured to determine whether any pathogenic organisms are present. These and other specialized medical problems underline the necessity for trained supervision.

Hastily conceived projects under lay direction are hazardous. Yet the emotional popular response to any publicity about eye-banks may lead to local undertakings, without adequate professional safeguards.

A major function of the eye-bank's national co-ordinating committee will be to supervise the development of new programs.

PURPOSES OF THE EYE-BANK

Ten years ago, when the eye-bank began its work, there was comparatively little interest in keratoplasty in the United States. Only some 15 surgeons in a few large centers were trained in this field, and precise information as to case selection was lacking. The principal bottleneck was the shortage of donor tissue.

The eye-bank therefore set these primary aims: to provide a supply of fresh or preserved corneal tissue to qualified eye surgeons throughout the country; to extend, by research and teaching, the skills requisite for corneal grafting; to develop a supply of salvaged eyes and corneal tissue for experimental research; and to stimulate research on the causes of blindness, particularly that arising from corneal disease or injury.

It was the basic premise of the program that, given the facts, people could be interested in donating their eyes after death and that surviving members of the family would honor the wishes of the deceased. The publicity appeal has proved effective. There has been a yearly increase in the number of donated eyes, as well as of excised pathologic eyes contributed by ophthalmologists. Some

3,800 eyes have passed through the eye-bank to date. Additional donor tissue made available through the eye-bank's publicity efforts has been allocated through branch banks or used locally with the consent of the bank.

Because of the rapid extension of keratoplasty, however, the demand for donor tissue still exceeds the supply. Several hundred eye surgeons are now performing corneal grafts.

The eye-bank is employing varied means to expand the supply of donor material. By arrangement with the Manhattan Eye, Ear, and Throat Hospital, where the eye-bank has its headquarters, when a donor living in any of the five boroughs of New York City dies in his own home, the enucleation of the eyes can be done there. Several resident eye surgeons at the hospital are available for this service. Under the procedure, the family physician notifies the eye-bank by telephone that death has occurred. The eyes are removed as soon as the death certificate has been signed and the permission of the nearest relative obtained.

In certain hospitals, when a patient is obviously dying, an intern suggests to the family the possible donation of his eyes for keratoplasty. Another method now under consideration is the development of a staff of trained interviewers who could talk with the families of the dead about such donation.

The eyes of the unclaimed dead are not available for keratoplasty since the law specifies a long delay prior to autopsy. While tissue from the eyes of electrocuted persons is usable as donor material, little effort is made to obtain it because of the sensational publicity attendant on securing the permission of the surviving family.

ORGANIZATION

The program of the eye-bank is a co-operative endeavor in which hospitals, voluntary agencies, transportation services, and the press take part. Wide publicity through mass communications media was indispensable to the launching of the program. On the whole, the press performed this service well,

although the occasional exaggerated or sensational news story raised false hopes among the hopelessly blind and caused temporary disaffection in some professional circles. While there was some question initially as to the optimum type of bank organization, the advantages of concentrating interest and support on a single co-ordinated program are now generally accepted.⁸

Co-operative arrangements had to be worked out with hospital staffs all over the country, on whom the bank must rely for such vital aid as obtaining the permission to enucleate from the next of kin after the death of a donor, performing the enucleation, and dispatching the eyes. A method had to be developed for rapid transportation of the perishable tissue. This is provided, free of charge, by the nation's air lines, particularly Eastern Air Lines, and the Red Cross Motor Corps, which transports the eyes to and from the airport as well as locally.

With the steady growth of the eye-bank program, the development of branch banks became feasible in areas where there was a large demand for keratoplasty. At this writing, the branches are operating in Boston, Philadelphia, Winston-Salem (North Carolina), New Orleans, Chicago, San Francisco, and Los Angeles. The branch unit receives eyes available in the area, distributing them locally as needed and sending surplus tissue to the New York center, which in turn allocates eyes to the branch units on request. The eye-bank handles the over-all publicity for the entire service. Close co-ordination between the various bank units will be fostered by the new national co-ordinating committee.

Our experience with the eye-bank program has shown the advisability of careful study prior to the opening of a branch bank. The anticipated demand for keratoplasty should be considered as well as the number of surgeons in the area qualified to do this surgery. If fewer than 100 grafts are likely to be performed in the course of a year, ample tissue should be available through the facilities of local hospitals and the New York bank.

EYE-BANK PROCEDURE

In its program for obtaining cadaver eyes, the eye-bank uses two permission forms. One, to be signed by a potential donor, expresses his wish to donate his eyes to the eye-bank, or, if he lives in an area with a branch bank, to the local institution. After he has signed the release and had his signature witnessed, the donor turns the form over to his spouse, nearest relative, or the person who will be in charge of funeral arrangements. After the death of the donor, the next of kin notifies the attending physician or the hospital authorities of the bequest and signs a permission form. His signature is legal authorization for enucleation.

A third form, designed for persons requiring enucleation for ocular pathology during life, authorizes the eye-bank to utilize such tissue for corneal grafting.

While, in the New York City area, the eye-bank has arranged for the removal of donated eyes at home when death occurs there, cadaver tissue is generally obtainable when the donor dies in a hospital. Removal of the eyes requires the same exacting care as in surgery on the living, and standard procedures must be followed in preserving the tissue. The New York bank supplies affiliated hospitals with permission forms to be signed by donors and family; instruction sheets describing procedures for the removal and preservation of eyes; history cards on which the surgeon enters pertinent information about the eyes; and educational material on the urgent need for donor tissue.

The services of the hospitals in removing and dispatching the eyes are free of charge. Immediately after the death of the donor, the eyes are carefully closed. The enucleation is done in the hospital operating room as soon as possible, preferably within two hours of death. Sterile surgical instruments must be used. The operative area is prepared as for any ocular surgery, care being taken to prevent soap, iodine, alcohol, or other cleansing preparations from running into the eyes. The conjunctival sac is copiously irrigated with

boric-acid solution or sterile saline.

The dissection is best done with scissors. The conjunctiva is dissected back from the corneoscleral junction, the extraocular muscles severed from the globe, and the optic nerve cut. The enucleated eye is placed in a sterile glass jar, fitted with a ground glass top, which was designed in the Eye-Bank Research Laboratory. The eye rests upright on a gauze square, saturated with sterile normal saline, which provides a moist atmosphere. The container is closed tightly and placed in a refrigerator at a temperature a few degrees above freezing until called for.

The surgeon then completes a history card which is attached to the container. He enters the age and sex of the donor, the cause, date, and hour of death, the death and hour of enucleation, information on any eye pathology that may be present, the results of Wassermann or other serologic tests, and any important laboratory findings.

The co-operating hospital notifies the eye-bank as soon as an eye is available. The bank then arranges with the Motor Corps of the Red Cross and, if the hospital is distant, with the air lines, for its delivery. When the period of transit is less than a half hour, the jar is transported in a cardboard container. For longer transportation, both jar and container are placed in a thermos container holding wet ice.

As soon as the container arrives in the bank, a technician records the information on the attached history card. The fluid in the glass jar is cultured. The globe is immersed for 10 minutes in aqueous merthiolate (1:5,000 in normal saline), then placed in a sterile glass jar. The eye rests upright on sterile cotton saturated in the same merthiolate solution. The jar is refrigerated at 4°C.

A surgeon experienced in all phases of corneal grafting examines each eye received at the bank with the slitlamp. He evaluates the actual condition of the cornea and the information on the history card, classifying the eye as: suited for penetrating keratoplasty; usable for a lamellar graft only; or

unsuitable for keratoplasty, to be used for research.

While tissue from donors of all ages may be used, I have found, on the basis of experience with several hundred corneal grafts, that the eyes of the elderly make superior graft material. Moreover, tissue from the very young, particularly prematures and infants, is extremely plastic, which presents operative difficulties. An adult eye, enucleated promptly after death, may be kept for as long as three days, if necessary, although children's eyes must be used sooner, and those of premature infants within 24 hours.

From research and clinical experience, guiding criteria for the selection or rejection of donor eyes have evolved. The donor cornea must be in good condition, free of secretion or local reaction. The donor must not have had an acute infectious disease. Under eye-bank procedures, eyes are selectively usable in the presence of certain types of ocular pathology, as follows: glaucoma simplex, if the corneal endothelium is not damaged; secondary glaucoma, but for lamellar transplants only, and provided the glaucoma has not arisen from a corneal ulcer. Eyes suspected of tumor are discarded, however, if there is marked aqueous flair and a turbid vitreous, since inflammatory tumor masses may be present. An eye with a tumor at the angle of the eye is rejected. Fuchs' dystrophy is, of course, a contraindication. A slitlamp examination of the cornea is particularly important when any corneal cloudiness is present to rule out the presence of this dystrophy on the corneal endothelium.

Eyes suitable for corneal grafting are sent at once to surgeons in need of them, the usual time interval between enucleation and the transplant operation being 48 hours. Freshly enucleated eyes are allocated to surgeons at the most distant hospitals.

Since the culture of the eye takes 24 to 48 hours, ordinarily the donor tissue is used before the bacteriologic report on it is available. The need for professional supervision of the bank is emphasized by the fact that

about half the eyes prove to be contaminated. If, for example, *Bacillus pyocyaneus* is found, the surgeon who used tissue from the eye must be informed immediately so that he can institute treatment. Prompt action may well avert loss of the patient's eye.

Among the organisms most frequently demonstrated are *Staphylococcus albus* and *Staphylococcus aureus*, both hemolytic and nonhemolytic, *Bacillus subtilis*, and diphtheroid bacilli; less common, streptococci, *Proteus vulgaris*, or *Diplococcus pneumoniae*. No particular precaution is necessary in the presence of nonpathogenic *Xerosis bacillus*, *Staphylococcus albus*, nonhemolytic, *Staphylococcus aureus*, or *Bacillus subtilis*. Antibiotic treatment must be instituted, however, if pathogenic organisms are demonstrated.

One development from the eye-bank program is the corneal clinic established by me at Manhattan Eye, Ear, and Throat Hospital some seven years ago. The clinic, which is held weekly, is open to people from the lower income brackets who have impaired vision resulting from corneal scarring. The examining surgeon dictates his findings on the type and extent of corneal scarring and the general condition of the eye to a specially trained secretary for immediate record. If a corneal graft seems promising, the patient is scheduled for surgery as soon as the preoperative preparation has been completed and a donor eye is available.

Statistical analysis developed⁴ on the results of keratoplasty in various diagnostic categories, together with published reports of other eye surgeons, serve as criteria for selecting cases favorable for corneal grafting. The data for the statistical analysis are drawn from special record cards maintained on all corneal graft cases. These cards, which now number several hundred, comprise a complete record of the preliminary diagnosis, operative course, and graft result.

In the course of the clinic's work, a number of teaching and resource materials have been developed. These include films of various

corneal graft techniques and a series of pre-operative and postoperative photographs on nearly all corneal graft cases.

Resident eye surgeons receive training in the techniques of corneal grafting through the facilities of the clinic and the Eye-Bank Research Laboratory. In addition, a concentrated course in this surgery is given to a selected group of ophthalmologists.

SUMMARY

From the perspective of 10 years' experience with the eye-bank program, certain conclusions are evident:

A co-ordinated national service offers several benefits. Available donor tissue is brought within reach of all qualified ophthalmologists. Financial support and the voluntary services of hospitals and transporta-

tion agencies can most effectively be enlisted through a single agency.

Any bank project, large or small, requires continuous professional supervision. Lay direction offers serious medical hazards.

The steady increase in the number of donated cadaver eyes has demonstrated that objective and realistic interpretation to the public can overcome prejudice against the removal of the eyes from the dead. On the other hand, sensational press stories, which occasionally appear, can prove damaging.

The eye-bank has stimulated the extension of keratoplasty in the United States, both in its primary role as a source of donor tissue and in its promotion of research and teaching.

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ANESTHESIA TECHNIQUES IN CATARACT SURGERY

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Since January, 1949, an effort has been made at the Charles T. Miller Hospital, Saint Paul, Minnesota, to arrive at some conclusions concerning optimal techniques of anesthesia in the surgery of senile cataract. These clinical investigations have been carried out, under supervision, by the residents in ophthalmology. The studies have embraced the fields of preoperative medication, including the use of some of the newer tranquilizing drugs, the employment of various types of local anesthetic agents, with particular emphasis on the use of Xylocaine, experience

with curare, results obtained from various combinations of anesthetics with spreading agents and vasoconstricting drugs, and, finally, variations in the technique of accomplishing the retrobulbar injection immediately prior to surgery. It is contemplated that detailed statistical data in support of the clinical impressions set forth in this communication will be published in the near future.

The principal justification for the continuing study of anesthetic procedures has been to ascertain prior to surgery the best possible

technique for each individual senile cataract extraction. It seems logical that, taking into consideration the type of cataract to be extracted and the method of surgery to be employed, an effort should be made to "tailor" the anesthetic and its mode of administration to the contemplated surgical procedure. It would indeed be naïve to suppose that ideal conditions of patient tranquility, motor block of the extraocular muscles, and intraocular pressure can invariably be achieved. It is contended, however, that by judicious pre-planning worthwhile strides toward such goals can be made. Experience has shown that they entail very little extra effort on the part of the operating room staff.

Before launching into a discussion of local anesthetic techniques, I feel it is possible to make a more or less categorical statement regarding patients who should have cataract extractions under general anesthesia, assuming that medical clearance for a general anesthetic can be obtained. There can be little disagreement that most psychotic, the extremely hard of hearing, and the markedly apprehensive patient are more easily handled under general anesthesia.

For general anesthesia at the Miller Hospital, we have used Baird's solution. This solution, first described by Baird in 1947, contains 25 mg. of sodium pentothal and 0.6 mg. per cc. of d-tubocurarine hydrochloride. Six-tenths milligram of curare is the equivalent of five units. All patients have had the benefit of endotracheal intubation carried out by an anesthesiologist.

It seems proper at this point to discuss the problem of the unduly apprehensive patient. Not infrequently some degree of anxiety can be traced to unfortunate surgical results which have occurred in friends or relatives. Some of these patients can be calmed by simple reassurance and perhaps a few words of explanation concerning the nature of the operation. It is well understood that some rather fantastic and lurid misinformation regarding the extraction of senile cataract has, over the years, gained

credence. There are, of course, a great many individuals who suffer from anxiety-tension states and who dread and fear the prospect of cataract surgery to the point that they will resort to almost any expedient to avoid an operation. In a relatively few instances we have placed such patients on a regimen of one of the newer tranquilizing drugs such as Thorazine or one of the rauwolfia compounds for at least two weeks prior to the day of operation. It must be acknowledged that the results to date have been rather disappointing. Many persons with anxiety-tension will, however, submit to surgery if a general anesthetic is employed. In fact, I have never refused to employ a general anesthetic in cataract surgery if the patient has insisted upon such a procedure.

From the standpoint of the operator, anesthesia with Baird's solution usually creates a favorable ocular status in most respects. Occasionally the eye assumes an awkward position of rest necessitating a superior rectus bridle suture. There can be little doubt that a very soft eye results from the use of Baird's solution. While this creates a desirable situation if an intracapsular extraction has been planned, it can cause definite embarrassment if an extracapsular operation is attempted or if the planned intracapsular extraction is unsuccessful. Under these circumstances it may become necessary to perform a complete iridectomy or to divide the sphincter, if a peripheral iridectomy has already been carried out. These modifications will usually result in successful completion of the lens extraction.

Postoperative nausea is not a frequent complication after the use of Baird's solution, especially when one of the anticurare-acting drugs, such as Tensilon, has been administered during the recovery period.

It is also highly important to occlude the lacrimal puncta temporarily after strong solutions of pilocarpine have been instilled in the conjunctival sac following the round-pupil operation. In my opinion insufficient attention has been paid to the effect of pilo-

carpine on the gastrointestinal tract as a cause of immediate postoperative nausea and vomiting.

Occasionally it becomes the rather unhappy responsibility of the ophthalmic surgeon to intervene because of postoperative complications which ensue a short time after the original extraction has taken place. Under these conditions it is sometimes difficult to obtain adequate local anesthesia because of the congested state of the globe. If such is the case, recourse to Baird's solution with endotracheal intubation is the best policy. I might say, parenthetically, that it has not been necessary to reoperate for failure of the anterior chamber to reform or because of a shallow anterior chamber since one-half percent eserine solution locally and Diamox orally have been used. This combination of drugs has been highly successful in our hands under these conditions, and we have not been obliged to inject either air or saline, or perform a sclerotomy since adopting this regimen.

Since my personal experience with curare and curarelike agents has not been extensive, I do not feel qualified to make any lengthy statement concerning their use. In a significant number of patients we have noted considerable anxiety after the administration of curare, despite the fact that very conservative dosages have been employed and an oxygen tube has been placed in close proximity to the nostrils. I would not and do not hesitate to use curare intravenously in suitable candidates if it is impossible to obtain an adequate motor block by means of retrobulbar anesthesia and an intracapsular extraction is strongly indicated.

Curare it has also been used in those rare circumstances where, upon completion of the corneal section, there has occurred a forward thrust of the iris-lens diaphragm indicating a "positive vitreous pressure." If an anesthesiologist is available and the requisite sterile equipment and oxygen are at hand, there will be no untoward delay while the patient is prepared to receive curare. On the

basis of my somewhat limited observations, I find it difficult, however, to visualize the necessity of using curare as a routine procedure in cataract surgery.

The majority of ophthalmic surgeons who perform surgery for the relief of senile cataract still employ some type of retrobulbar injection together with O'Brien or Van Lint-Rochat akinesia or some modification thereof. Various topical anesthetics such as cocaine, dorsacaine, or pontocaine are ordinarily instilled in the conjunctival sac before the infiltration agents are administered. Prior to September, 1952, I had always employed one or two-percent novocaine with or without epinephrine for akinesia and retrobulbar injection. For the last three years, however, I have used, at first two-percent and more recently one-percent, Xylocaine for these purposes. The anesthetic is used in combination with epinephrine alone or with hyaluronidase added, depending upon the type of operation to be performed.

If an extracapsular extraction is in prospect, one-percent Xylocaine or two-percent novocaine is used in the retrobulbar injection. The 25-gauge, 3.5 cm. needle is used to inject 1.5 cc. of novocaine or Xylocaine. As a rule this will not bring about a sufficiently great fall in tension to jeopardize the capsulotomy procedure.

On the other hand, if a very soft eye and a highly effective motor block are desired to permit every possible opportunity for the successful extraction of the lens in its capsule without complications, then five to 15 units of hyaluronidase per cc. of one-percent Xylocaine containing epinephrine 1:100,000 should be injected.

In our experience the method of injection suggested by H. Gifford, employing a 25-gauge 5.0-cm. needle, will give a higher percentage of ideal motor blocks than if the shorter needle employing the Atkinson technique is used. It must be admitted, however, that the use of the Gifford technique carries with it a greater risk of retrobulbar hemorrhage. We no longer use the long 5.0-cm.

needle in markedly hypertensive and/or markedly arteriosclerotic patients.

Except for a very recent instance of hysterical amblyopia which occurred during the course of a retrobulbar injection, I have not observed any complications from retrobulbar anesthesia except that of orbital hemorrhage. Even a minor hemorrhage necessitates postponement of surgery for at least several weeks. We have made it a rule not to repeat the injection behind the globe when the patient returns for surgery but to use a general anesthetic.

There is very little that need be said about preoperative medication. Nearly every ophthalmic surgeon has his favorite preoperative drug and, since it is virtually a universal custom to give the patient a trial the evening before operation with the same drug that is to be employed as a sedative an hour or so immediately prior to surgery, there should be a minimum of serious complications from this important detail.

A paradoxical effect from barbiturates in elderly patients is perhaps the most common difficulty which I have encountered. Demerol, chloral hydrate, barbiturates, and some of the newer nonbarbiturate sedative drugs have all been employed from time to time, although currently we are using 50 or 75 mg. of Demerol both the evening before and one hour before operation in the morning.

There has been some discussion regarding the relative merits of novocaine and Xylo-

caine as infiltration anesthetics. There can be little doubt that both are highly satisfactory for ophthalmic surgery. I prefer Xylocaine because it is my impression that in a one-percent solution it produces a profound local anesthesia of the lids and globe and a somewhat higher percentage of satisfactory motor blocks. I have never experienced an untoward local or general reaction with Xylocaine, although such reactions have been reported. I have, however, witnessed several generalized and serious reactions after novocaine injections.

Xylocaine is stable in aqueous solution to a greater extent than any other commonly used local anesthetic. It apparently acts more rapidly than novocaine, but its effect is of sufficient duration to permit the completion of even a prolonged cataract extraction. Even without massage through the upper lid following injection, a satisfactory motor block will have become established within seven or eight minutes after the needle is withdrawn from the retrobulbar space. If at the end of this time an adequate block cannot be demonstrated, another retrobulbar injection should be carried out or intravenous curare administered. Finally, Xylocaine possesses some slight degree of vasoconstricting power, while novocaine has the opposite effect. Thus smaller amounts of epinephrine may be employed with Xylocaine than with novocaine.

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GLIAL TUMORS OF THE RETINA*

IN RELATION TO TUBEROUS SCLEROSIS

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It seems particularly fitting, in contributing a paper to the volume honoring Dr. Alan C. Woods, that I who started residency training under him the day he began his professorship should present a corollary to the first paper which I wrote under his tutelage. That paper reported a case of astrocytoma of the retina.¹ It is the purpose of this paper to review that case and to record two other cases of astrocytic retinal tumors encountered since then. Consideration of these three unusual tumors as a group raises the question of the part played in them by tuberous sclerosis.

This condition, also known as "epiloia" or "de Bourneville's disease," is a hereditary condition with many manifestations and variations. It has been grouped by van der Hoeve² as one of the phakomatoses.

Van der Hoeve's original papers²⁻⁴ and the reviews by Walsh,⁵ Reese,⁶ and Duke-Elder⁷ cover the literature and the general manifestations of tuberous sclerosis. The complete disease picture includes: multiple astrocytic nodules of the cerebrum, resulting in epileptiform seizures and mental retardation; retinal tumor masses; tumors of various viscera, especially the heart and kidneys; and adenoma sebaceum of the face, often appearing at puberty. However, the majority of the cases reported are incomplete manifestations of the total complex.

The three cases to be discussed appear to represent partial forms of the disease.

CASE REPORTS

CASE 1

This case has been described previously in detail.¹ A 23-year-old white woman with neg-

ative familial and past history had an eye removed in 1936 for a large, whitish intraocular tumor in the posterior pole. The other eye was normal. There was no evidence of neurologic, cutaneous, or visceral disease. Histologic examination showed that the tumor was composed for the most part of astrocytes with long fibrillary processes. There were also scattered clumps of large irregular cells with abundant cytoplasm and round or oval nuclei, a few of them multinucleated. The tumor was confined to the retina; it appeared to originate in the inner layers but in some areas replaced the entire retinal thickness.

Follow-up study on this patient was made by Dr. Frank B. Walsh this spring (1955), 19 years after enucleation. She is living and well, with no evidence of tumor recurrence and no evidence of disease of visceral, cutaneous, or central nervous systems.

CASE 2

A six-month-old white girl had an eye removed in 1942 for retinal tumor thought to be retinoblastoma. At the time of enucleation the child's physical examination was negative except for convulsive seizures which were felt to be idiopathic epilepsy. Family history was entirely negative.

Section of the tumor, which was close to the nervehead, showed it to be entirely retinal, apparently arising from the inner layers but spreading to replace the whole retinal thickness in some areas. The tumor (fig. 1) was composed of astrocytes with an abundance of fibrillary processes (fig. 2). Silver stains were suggestive of astrocytic "sucker feet" about the blood vessels, which were not numerous. Very occasionally a large cell with clear eosinophilic cytoplasm and large nucleus was seen.

* From the Department of Surgery (Ophthalmology) of the New York Hospital-Cornell Medical Center. Presented at the 91st annual meeting of the American Ophthalmological Society, June 3, 1955.



Fig. 1 (McLean). Case 2. Lower-power photomicrograph of retinal tumor. (Trichrome stain.)

Follow-up on this child 13 years later finds her in a home for the mentally defective. She is a complete idiot, totally unable to care for or even feed herself. She is still having frequent epileptiform seizures. She has begun to menstruate and develop secondary sexual characteristics. With these have come early skin changes on the face and upper trunk resembling adenoma sebaceum. There are no clinical signs of cardiac or renal lesions. Recent laboratory studies have not been obtained.

CASE 3

Within the past year a nine-month-old white girl of normal, nonconsanguineous parents was found to have a tumor in the periphery of her retina. Family history was negative except for two older brothers who are said to have simple strabismus but to be otherwise normal. The child had been somewhat retarded in her development and began to have mild convulsive seizures at the age of six months.

Physical examination disclosed a well-developed female child with evidence of early

cerebral dysgenesis. Electroencephalograms showed a grossly pathologic pattern without

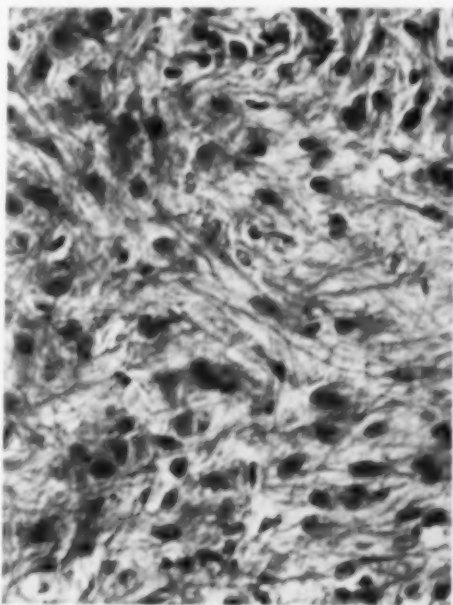


Fig. 2 (McLean). Case 2. Photomicrograph, showing astrocytic fibrils. (Trichrome stain.)



Fig. 3 (McLean). Case 3. Photomicrograph of retinal tumor. (Hematoxylin and eosin.)

focus. X-ray studies of the skull were negative. An electrocardiogram showed an absence of the isoelectric phase of the ST segment although clinical examination of the heart was negative. Intravenous pyelography and urine studies were normal. There were no skin lesions.

Before all of these studies had been made, a clinical diagnosis of retinoblastoma was concurred in by several consultants, and the eye was enucleated. In this case the tumor was smooth, whitish, peripherally located, and moderately elevated. On histologic study it was found to be composed of astrocytes similar to those of the other two cases (figs. 3 and 4). It also contained a few large clear cells.

COMMENT

All three of these cases are cytologically similar and represent primary astrocytic retinal tumors. All are differently located: Case 1 at the posterior pole, Case 2 near the optic nerve, Case 3 at the ora serrata. All are in white females, one at the age of 23 years, two under one year. None was correctly diagnosed clinically. Case 2 fits the criteria for

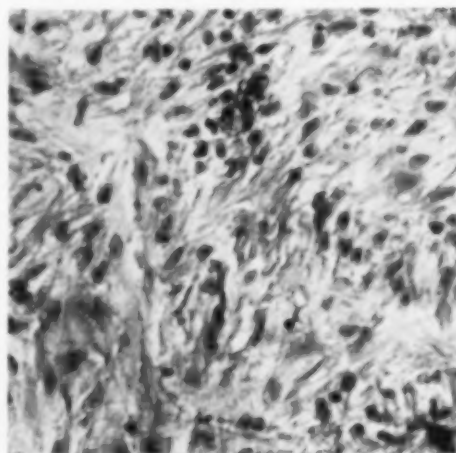


Fig. 4 (McLean). Case 3. Photomicrograph, showing cell detail. (Phosphotungstic acid-hematoxylin.)

a diagnosis of tuberous sclerosis rather well. Case 3 gives enough evidence, including the possibility of a cardiac tumor, for presumptive diagnosis. Case 1 shows no evidence of the syndrome but the retinal tumor.

All three of the retinal tumors are solid whitish masses of smooth contour without

the mulberry shape, the cystic appearance, or the seeding characteristics usually seen in the retinal lesions of tuberous sclerosis. All appear cytologically to be relatively benign, and none has shown evidence of recurrence or metastasis. None showed calcium deposition. There were no drusen in the optic nerves.

Reconsideration of the histologic studies of the retinal masses of tuberous sclerosis available in the literature⁸⁻¹² indicates that all of them are basically similar and that all the tumors are apparently astrocytic. Reese¹³ has pointed out the similarity of drusen of the optic nerve to the ocular lesions of proven tuberous sclerosis and indicated their astrocytic nature. Chambers and Walsh¹⁴ have discussed drusen of the optic nerve and emphasized their frequency as isolated phenomena. If we are to accept the suggestions made by Reese¹³ and Koch and Walsh,¹⁵ among others, that diagnosis of tuberous sclerosis in forme fruste is to be made on the finding of ocular lesions alone, and that drusen of the nerve represent such disease, then this entity is, in incomplete form, much more common than is usually realized.

The interrelationship of tuberous sclero-

sis and the more common von Recklinghausen's neurofibromatosis must also be considered. The frequent association of astrocytic gliomas of the optic nerve with this latter symptom complex is known,^{16, 17} and van der Hoeve has pointed out that ophthalmoscopically similar retinal tumors may be seen in each. Indeed, Verhoeff,¹⁸ studying optic nerve tumors, predicted the finding of retinal astrocytoma before the first one was reported. Hogan¹⁹ has recently seen a retinal tumor, not unlike the ones reported here, in a case of von Recklinghausen's disease. Cutaneous neurofibromas and cafe-au-lait spots are sometimes found in tuberous sclerosis.

What conclusions are we to draw? Is tuberous sclerosis in incomplete form a relatively common disease? Does it really overlap von Recklinghausen's syndrome? Might we not do better to characterize such lesions as we find in individual cases without trying too hard to pigeon-hole them in complex categories? However, we must not forget completely the implications of the potential hereditary factors.

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CONGENITAL FIBROSIS OF THE EXTRAOCULAR MUSCLES*

A REPORT OF SIX CASES

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Fibrosis of one or two of the extraocular muscles, producing a strabismus fixus, is not uncommon. The most frequent and best known example of this is Duane's syndrome. Fibrosis of both internal recti, resulting in a bilateral convergent strabismus fixus, is also occasionally seen, although infrequently.

The purpose of this paper is to report six unusual cases of congenital fibrosis of all the extraocular muscles presenting a rare syndrome of complete strabismus fixus which has been called general fibrosis syndrome by Brown,[†] who describes three similar cases. Five of the cases reported here have been treated surgically by me.

The characteristic features of this syndrome are:

1. Fibrosis of all extraocular muscles.
2. Fibrosis of Tenon's capsule.
3. Adhesions between muscles, Tenon's capsule, and the globe.
4. Inelasticity and fragility of the conjunctiva.
5. No elevation or depression of either eye.
6. Little or no horizontal movement.
7. Both eyes fixed in a position of downward gaze 20 to 30 degrees below the horizontal.
8. Bilateral ptosis.
9. Headtilt backward with chin elevated.
10. The condition is present at birth.

* From the Department of Ophthalmology, Children's Orthopedic Hospital.

† Brown, H. W.: In Allen, J. H.: *Strabismus Symposium*, St. Louis, Mosby, 1950, Chap. XI, p. 229.

REPORT OF CASES

CASE 1

H. B. was first seen when 11 years of age. He had been referred to the orthopedic clinic because of poor posture. Examination showed both eyes in a position of downward gaze of approximately 30 degrees (fig. 1A). There was no vertical movement in either eye. A variable divergent strabismus was present: the right eye deviating outward approximately 10 degrees when fixing with the left eye and the left eye deviating as much as 40 degrees when fixing with the right eye. There was practically no inward rotation of either eye, slight outward movement of the right eye, and somewhat more outward rotation of the left eye. Bilateral ptosis was present with little or no levator action.

The following surgical procedures were performed at approximately two-month intervals:

Operation 1. Recession inferior rectus, right eye, seven mm. Exploration superior rectus.

Operation 2. Sling suture for ptosis, right eye.

Operation 3. Recession inferior rectus left eye seven mm. Advancement superior rectus left eye four mm.

Operation 4. Sling suture for ptosis, left eye.

Operation 5. Sling suture for ptosis, right eye (inadequately corrected by first ptosis operation).

All four rectus muscles operated on or ex-



Fig. 1A (Laughlin). Case 1. Preoperative. Note backward tilt of head, downward gaze of eyes, and ptosis.

explored were fibrotic and tight, with no elasticity. They were adherent to the globe and Tenon's capsule and the dissection was difficult. The conjunctiva was inelastic and fragile. There was more than average postoperative edema after each of the muscle procedures. The end result was satisfactory (fig. 1B), although the right eye was still down about 10 degrees more than the left eye and binocular vision was not present. He used the right eye for reading and close work and the left eye for distant vision. There was



Fig. 1B (Laughlin). Case 1. Postoperative. Note improvement in position of head, as well as position of eyes and lids.

considerable improvement in the divergent strabismus. Following the sling suture in the left eye, there was a recurrent superficial ulceration of the cornea at the lower limbus for approximately six months. There has been a marked improvement in his posture.

CASE 2

T. M. was first seen at the age of six and one-half years. Both eyes were fixed in a position down and to the left, approximately 25 degrees down and 15 degrees to the left. There was no movement in any direction in either eye and bilateral ptosis was present. There was no appreciable defect in his posture (fig. 2A). Family history revealed the same condition present in one brother (Case 3), the mother (Case 6), the maternal grandmother, great grandfather, and several other members of the family. The following surgical procedures were done at approximately two-month intervals:

Operation 1. Recession inferior rectus, right eye, six mm. Resection superior rectus four mm., and advancement superior rectus four mm., right eye.

Operation 2. Sling suture ptosis, right eye.

Operation 3. Recession inferior rectus, left eye, six mm. Resection superior rectus four



Fig. 2A (Laughlin). Case 2. Preoperative. Note backward tilt of head in order to look at camera, downward position of eyes, and ptosis.



Fig. 2B (Laughlin). Case 2. Postoperative.

mm., advancement superior rectus four mm.

Operation 4. Recession internal rectus, right eye, and tenotomy external rectus, left eye.

Operation 5. Sling suture ptosis, left eye.

As in the previous case, all muscles were fibrotic, inelastic, and adherent to the globe and Tenon's capsule. It was sometimes difficult to identify muscle tendon from the dense fibrotic Tenon's capsule. The conjunctiva was thick, fibrotic, inelastic, and bled easily. Postoperative reaction was moderate. No ulceration of the cornea was noted. Figure 2B shows the final result.

CASE 3

R. M., brother of the patient in Case 2, was first seen when two years of age. The eyes were fixed in downward gaze of 30 degrees and marked bilateral ptosis was present (fig. 3A). There was no movement of the right eye in any direction; the left eye showed limited internal rotation, otherwise no movement. The head was tilted far backward but no postural defect was noted. The following operative procedures were performed over a period of one and one-half years:

Operation 1. Recession inferior rectus, right eye, six mm. Advancement superior rectus, right eye, four mm.

Operation 2. Recession inferior rectus, left eye, eight mm. Advancement superior rectus, left eye, four mm.

Operation 3. Recession external rectus, right eye, 4.5 mm. Resection internal rectus, right eye, three mm. Advancement internal rectus, right eye, two mm. Blascovitz's operation for ptosis, left eye.

Operation 4. Blascovitz's operation for ptosis, right eye.

Operation 5. Sling suture ptosis, right eye.

All operated muscles showed the abnormalities as noted in previous cases. A divergence of the right eye was not evident before



Fig. 3A (Laughlin). Case 6 and Case 3. (Left) Case 6, mother of patients in Cases 2 and 3. (Right) Case 3. Preoperative. Note extreme backward tilt of head.



Fig. 3B (Laughlin). Case 3. Postoperative.

the eyes were elevated but may have been present. After the second operation a divergence of approximately 15 degrees was noted. For some unexplainable reason both eyes were elevated before the ptosis of either eye was corrected so that both pupils were covered by the lid. At this stage it was rather amusing to see him elevating one lid with his hand and energetically handling toys with the other hand. The handicap was surprisingly slight. Final result is shown in Figure 3B.

CASE 4

P. P. was 13 years of age when first seen. Both eyes were in a downward position of approximately 40 degrees with no elevation or depression in either eye. There was a divergence of approximately 30 degrees with fair lateral movement. Bilateral ptosis was present and the head was tilted backward (fig. 4A). The condition had been present since birth and there was no familial history of eye disease. The following operative procedures were done over a period of two years:

Operation 1. Recession inferior rectus, right eye, five mm. The eye seemed in good position vertically for about two weeks after the operation; then gradually came down almost to the original position.



Fig. 4A (Laughlin). Case 4. Preoperative.

Operation 2. Resection superior rectus, right eye, five mm. Advancement superior rectus, right eye, four mm. Recession external rectus, right eye, five mm.

Operation 3. Sling suture ptosis, right eye.

Operation 4. Recession inferior rectus, left eye, six mm. Resection superior rectus, left eye, five mm. Advancement superior rectus left eye, three mm.

Operation 5. Sling suture ptosis, left eye. (Very little improvement in ptosis, still variable divergent strabismus up to 30 degrees.)

Operation 6. Tenotomy external rectus, right eye. Resection internal rectus, right eye, five mm.

Operation 7. Removal of sling suture left eye because of infection along suture.

Operation 8. (Two months after Operation 7.) Sling suture ptosis, left eye.

Operation 9. Recession external rectus, left eye, eight mm.

Operation 10. Tightening of sling suture, left eye. (Suture knot was isolated and re-tied shortening the suture approximately 12 mm.)

This was the most difficult case in the series and the final result was not entirely satisfactory but is actually better than indicated by the photograph (fig. 4B). All mus-



Fig. 4B (Laughlin). Case 4. Postoperative. Note improvement in position of head and eyes. Ptosis is undercorrected.

cles operated were fibrotic except the left lateral rectus which did not appear fibrotic but was tight and inelastic. Corneal ulcers developed in both eyes after correction of the ptosis but were not severe. Infection along the tract of the first sling suture in the left eye was probably from a severe acne. Antibiotics were not used until the infection developed. However, antibiotics were used prophylactically after the second and third ptosis operations on the left eye and no infection developed.

CASE 5

A. T. was first seen at the age of 10 and one-half years. Examination showed both eyes fixed in a downward position of approximately 40 degrees and each eye diverging approximately 10 degrees. There was absolutely no movement of either eye in any direction. Marked bilateral ptosis was present (fig. 5A). The condition had been present since birth and family history was negative with regard to eye anomalies. The following operative procedures were performed at intervals of one week.

Operation 1. Recession inferior rectus, right eye, six mm. Resection superior rectus,



Fig. 5A (Laughlin). Case 5. Preoperative.

right eye, six mm. Tenotomy superior oblique, right eye. (The superior oblique was also fibrotic and was adherent to the superior rectus. The insertions to the globe were adjacent and it was impossible to separate the muscles, consequently tenotomy of the superior oblique was done in order to isolate the superior rectus.)

Operation 2. Sling suture ptosis right eye. Recession inferior rectus, left eye, six mm. Resection superior rectus, left eye, six mm. (The insertion of the superior oblique was



Fig. 5B (Laughlin). Case 5. Postoperative, six days after third operation and three weeks after first operation.

beside and continuous with the insertion of the superior rectus, but it was possible to separate the muscle, more or less, and the superior oblique was left intact.)

Operation 3. Sling suture for ptosis, left eye.

The muscles, Tenon's capsule, and conjunctiva in this case were the same as in the previous one. The end result is shown in Figure 5B.

CASE 6

M. M. (fig. 3A), mother of the patients in Cases 2 and 3, was examined but not treated surgically. The eyes were in downward position of approximately 15 degrees. No elevation or depression was present but five to 10 degrees lateral movement was possible in each eye. Bilateral ptosis with minimal levator action. However, the cosmetic appearance was not unattractive and surgical treatment was neither desired nor advised. No postural defect was present.

DISCUSSION

The similarity of the cases is striking. All six cases exhibited all the characteristic features noted. The etiology other than congenital malformation is unknown. The dense adhesions and fibrosis of Tenon's capsule and changes in the conjunctiva would suggest a prenatal inflammatory disease but the occurrence of the syndrome in four successive generations (Cases 2, 3, and 6) precludes this as a possibility.

A biopsy of the inferior rectus muscle was done in Case 5. This was taken from the side of the muscle as far back as possible and well beyond the tendon. The pathologic report was "Section shows some parallel bundles of hyalinized collagen enclosed in dense fibrous tissue. No muscle tissue seen."*

* The sections on this biopsy were not completed in time to include a photomicrograph or any special studies in this paper. They will be reported later. The pathologic report was by a general pathologist.

It is recommended that the surgical procedures be carried out in the following order:

First operation, elevate one eye.

Second operation, elevate second eye and correct ptosis in first eye.

Third operation, correct ptosis in second eye.

Combined ptosis and muscle surgery is not recommended due to the unusual amount of postoperative reaction following muscle surgery; and, furthermore, one cannot be sure that the eye will remain in the same position as on the operating table. Therefore, the needed amount of ptosis correction is uncertain. A recession of the inferior rectus alone does not give adequate elevation, although on the operating table this appears to be sufficient, consequently some kind of shortening operation on the superior rectus is necessary. I believe that more vertical correction is obtained when the two procedures are done as a single operation than if done separately.

If the ptosis is not corrected in the first eye before or at the same time the second eye is elevated the patient will not be able to see without manually elevating one lid. The Guyton-Friedenwald sling suture is recommended for correction of ptosis. The condition of the levator muscle is unknown and the amount of correction obtained by levator shortening is uncertain.

The Blasovitz procedure was quite successful on one eye in Case 3 but failed completely on the second eye. This may have been due to faulty operative technique as the muscle appeared the same in both eyes. Very little levator muscle could be definitely identified but there was no dense fibrosis of the muscle and capsule, as was anticipated.*

Care must be taken not to overcorrect the ptosis as the eyes do not roll upward during sleep and the cornea may be considerably exposed during sleep. It is recommended, therefore, that the upper lid be elevated just above the center of the pupil for functional

result only, rather than to the upper limbus which would be ideal cosmetically. Two of the cases (1 and 4) did develop superficial ulceration of the cornea after ptosis surgery but both eventually cleared without scarring. In event the ulceration should persist the sling suture can easily be removed but it is rather difficult to undo a levator shortening operation.

SUMMARY

Six reports of cases of congenital fibrosis of all the extraocular muscles are presented. All cases exhibit the 10 features characteristic of this syndrome. Five of the six cases were operated with marked cosmetic improvement. The suggested operative routine is discussed.

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OCULAR MOVEMENT*

I. MECHANICS, PATHOGENESIS AND SURGICAL TREATMENT OF ALTERNATING HYPERTROPIA (DISSOCIATED VERTICAL DIVERGENCE, DOUBLE HYPERTROPIA) AND SOME RELATED PHENOMENA

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I. PURPOSE OF PAPER

Alternating hypertropia appears paradoxical both at first glance and at second glance. This paper proposes to resolve this apparent paradox by correlating two concepts (or theorems) which appear essentially self-evident after receiving sufficient attention, but which are not readily visualized even separately, let alone in combination. Our explanation points out how surgical procedures can be planned to correct deviations which are oppositely directed, or unequal in degree, on alternate fixation. We have found surgery for correcting alternating hypertropia to be rather successful.

These concepts can likewise explain differences in the degree of horizontal squint

according to which eye is fixating, when refraction and accommodation are equal, although we do not consider such differences important. Despite our inability to present the picture more clearly and coherently, we hope some readers will find it worthwhile to wade through this paper in detail sufficient to grasp the concepts in full, and to explore other ramifications. We realize this may not be easy.

II. PHENOMENA OF ALTERNATING HYPERTROPIA

Bielschowsky¹ introduced the term "dissociated vertical divergence" to designate a type of vertical extraocular muscle imbalance wherein the visual axis of one eye deviates from that of its fellow in an alternately opposite upward or downward direction, depending on which eye is fixating and which is dissociated (fig. 1). (For comparison, Figure 2 illustrates a "simple" hypertropia, where the vertical deviation remains the same regardless of which eye is fixating and which is dissociated.) Other names for this phenomenon include alternating hypertropia, alternating hyper-

* From the Department of Ophthalmology of the Henry Ford Hospital. This is the first of a series of papers which are based on work begun in 1950 at the Wilmer Institute of The Johns Hopkins Hospital and University and since continued at the Henry Ford Hospital. Subsequent reports in this series will be submitted at irregular intervals. Some of the material in this particular paper was presented in preliminary form at the 11th Clinical Meeting of the Wilmer Residents Association on April 3, 1952.

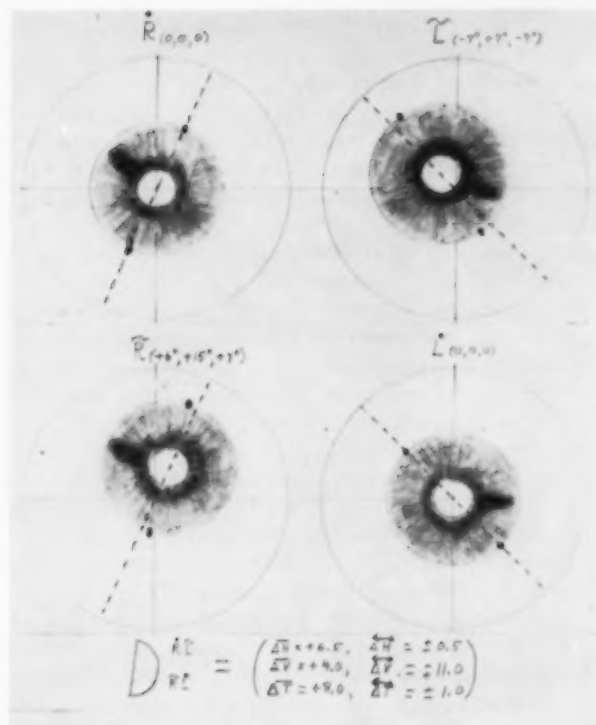


Fig. 1 (Guyton and Kirkman). A typical case of alternating hyperopia. Upper diagrams show the right eye fixating in its primary direction, while the left eye is dissociated and deviates medially, upward, and extorsionally. Lower diagrams show the left fixating in its primary direction, while the right eye now is dissociated and deviates medially, upward, and extorsionally. Measurements taken from serial photographs. The broken lines indicate the respectively proper reference planes from which torsional rotations of the deviated eyes should be measured. The symbolic representations of position and deviation are explained later on in the text.

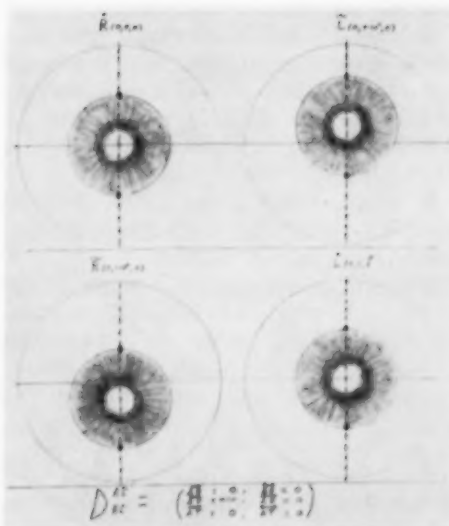


Fig. 2 (Guyton and Kirkman). "Simple hyper."

phoria, anomalous vertical divergence, occlusion hypertropia, anaphoria or kaptropia, alternating sursumduction, or simply double hyper, which is the term probably used most widely in everyday parlance.

While we choose to regard the above designations as synonymous, it should be pointed out that authors differ somewhat as to which cases should be included under one or another of these designations. Thus, cases where significant alternate vertical deviations largely or completely disappear when a concurrent horizontal squint is compensated for may or may not be classified differently. Also, cases with alternate vertical deviations of small degree for alternate primary fixation, but with oppositely directed vertical deviations of large degree on looking right and looking left regardless of which eye is fixating, may or

may not be designated differently. To avoid confusion, we will undertake to explain all such variations, although at least the last one mentioned does not fall into the exact category defined at the beginning of this section.

Double hypertropia is quite common. Bielschowsky found it in 41 percent of his cases with amblyopia, and an unstated but very appreciable percentage of his other cases. Other careful observers have found the incidence to be of this approximate magnitude. When double hypertropia is present to any considerable degree, it has generally been considered to impart a poor prognosis for single binocular vision, unless it can be largely alleviated by correction of any concurrent horizontal deviation. No other surgical treatment has been recommended for double hypertropia.

Deviation of the dissociated eye is usually upward, but in rare cases it is downward. An appreciable moment-to-moment variation in the extent of the vertical deviation, even while the same eye is fixating, is common. In cases where there is binocular fusion part of the time, one often sees alternate vertical deviations of from five to 10 degrees, which amounts to several times the magnitude of normal vertical vergence powers. Most often, there is some asymmetry in the amounts of hypertropia exhibited by the two eyes when they are alternately dissociated. There usually is some horizontal deviation (internal or external), which may be great or may be inconstant and hardly perceptible. There is regularly a torsional deviation, usually extorsional (excyclovergent) of very appreciable degree, although this often escapes attention unless observations are made with better illumination and magnification than are customary for cover testing.

We have seen intorsional deviation associated with downward deviation of the dissociated eye in two cases. Verhoeff² reports having seen an intorsional deviation

associated with upward deviation of the dissociated eye in two cases. The large majority, however, show an extorsional deviation, which may vary in degree but remains extorsional regardless of which eye is fixating and which is dissociated, with upward deviation of the dissociated eye.

Our experience with double hypertropia has closely paralleled that of Verhoeff. Of his 42 cases, there were only five without horizontal deviation of appreciable degree, either manifest or under cover, or a history of manifest horizontal squint sometime previously. Upward deviation of the covered eye was associated with extorsion in all but two of his cases, although in some of these the upward movement was so slow he could only demonstrate the extorsion by the fact that intorsion occurred in the return movement, when the eye was uncovered. In the two exceptions, upward deviation of the covered eye was associated with intorsion, as mentioned above. In nine of his cases there was nystagmus, and in four of these the nystagmus was rotary. Finally, 13 of his cases had amblyopia ex anopsia (20/50 to 1/200).

While double hypertropia generally varies somewhat in degree and symmetry according to the positions of gaze, in general it will still show up to a greater or lesser extent regardless of (1) the direction of gaze, (2) the use of prisms and (3) the use of any other lenses which may be needed for equalization of accommodation-convergence stimuli from the two eyes. A quantitatively asymmetrical double hypertropia at any given fixating position (for example, for the primary position) may conveniently be regarded as a symmetrical double hyper combined with a "simple" or "average" hypertropia of lesser degree (fig. 3) or of greater degree (fig. 4). If the simple hyper component ΔV is greater than the double hyper component ΔV , on alternate fixation there is merely a difference in degree rather than an actual rever-

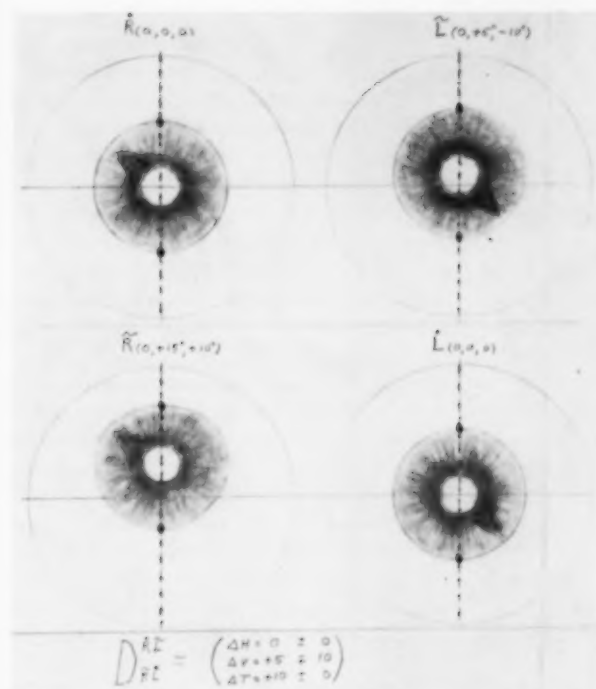


Fig. 3 (Guyton and Kirkman). A symmetrical double hypertropia, where the oppositely directed vertical component is greater in magnitude than the average ("simple") vertical component (that is, $|\Delta V| > |\overline{\Delta V}|$, in terms of symbols used later). Somewhat idealized, neglecting any horizontal deviations.

sal of direction of the vertical deviation. In such a case, utilization of an appropriate prism to compensate for the average component of vertical deviation $\overline{\Delta V}$ will "unmask" the oppositely directed components of the double hypertropia.

The demonstration of double hypertropia predicates an ability of each eye at least to make an attempt at monocular fixation when the other eye is covered. However, there are cases of nonalternating squint with marked amblyopia of one eye, where covering the squinting eye causes it to move further upward, or even to initiate the upward deviation, whereas gradually obscuring the fixating eye with a darkened wedge causes the uncovered amblyopic eye to move downward, to a level with or below that of the dominant eye. This is known as the Bielschowsky phenomenon, and such cases are properly classed in the category of double hypertropia.

A glance at the list of synonyms for double hypertropia suggests an argument over whether the customary division of manifest or latent squint into *tropias*, if deviations are constantly or intermittently present in everyday life, and *phorias*, if the deviations appear only when one eye is artificially dissociated by screening or some other means of preventing its receiving sufficient stimulus to fixate, should apply in these cases. Lancaster³ objected to any use of the term "phoria" for cases of double hypertropia, on the grounds that the vertical deviations of the alternately covered eyes are not comitant. For the different reason that the dissociated eye regularly suppresses during dissociation, whether artificially induced or not, we too would consider it more proper to designate these cases as *tropias*, regardless of how infrequently dissociation occurs during everyday life.

Some patients with double hypertropia bifixate (fuse) most of the time during

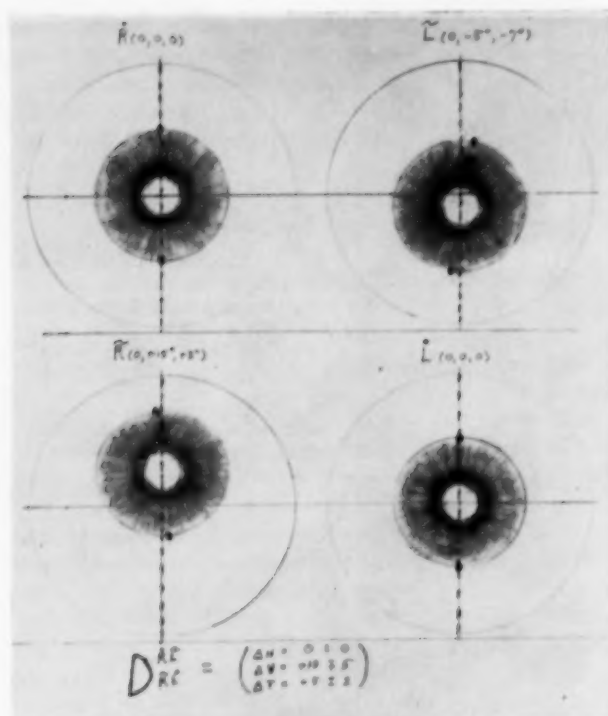


Fig. 4 (Guyton and Kirkman). Asymmetrical double hypertropia where the average ("simple") component exceeds the oppositely directed vertical component during alternate fixation in the primary direction (that is, $|\Delta V| < |\Delta V|$). Again no horizontal deviations are shown.

ordinary day-to-day use of the eyes, and others bifixate some smaller portion of the time. In such cases, upward deviation of one or of alternate eyes is more likely to appear with fatigue. Also, if the object (target) receiving visual attention is completely blocked from the view of one eye or the other, that eye will deviate (for example, rotate upward and extort). Often this will happen if the view is only partially blocked, or the image is sufficiently blurred by interposition (for instance) of a strong plus lens or dimmed by means of a plain dark lens. Lessened contrast of the details in the image to an eye, rather than reduction in the amount of light entering the eyes, appears to be the principal factor in determining whether the eye will "dissociate" and deviate: a diffuse, dazzling background illumination supplied to only one eye is likely to cause that eye to dissociate in a case of this sort.

If there is an appreciable "dominance" of one of the two eyes, the dominant eye will be used for fixation during most of the everyday life situations where there is not bifixation. If dominance is very pronounced, the eye used less often for fixation likely will be slightly or markedly amblyopic. In cases with double hypertropia, if there is ability to bifixate (either without or with the aid of prisms or a major amblyoscope), dissociation of the poorer eye can be induced by a small reduction in the relative attention value of its visual stimulus, whereas dissociation of the dominant eye instead requires a large reduction in the relative attention value of its retinal image stimulus. This applies to cases of double hypertropia whether there is bifixation ability or not, and is readily demonstrated with a major amblyoscope, where the relative attention values of the two targets can readily be

controlled by varying the illuminations, flashing one or the other, and so forth.

In some cases of alternating hypertropia with little or no detectable dominance of one eye over the other, determination of which eye shall fixate appears subject to some measure of conscious control. Exactly how conscious effort can (apparently) enhance the attention value of image stimuli of the one eye or the other is interesting from a speculative standpoint, but is not material to the purpose of this paper.

The difficulty in observing torsional rotation, as compared with seeing vertical and horizontal movements, can very readily be shown by taking a moving picture film of a case of double hypertropia, utilizing differing magnifications and illuminations. It need repeatedly be emphasized that torsional movement is not often recognizable unless the eyes are observed under conditions of much brighter illumination than are usually used, and are observed from very close range, and from such a position that each eye in turn can be watched while it is being covered and uncovered. On alternate cover, the return movements are often so rapid that torsional rotation cannot be recognized if the eye is not visible to the observer until it is uncovered. Moving picture sequences taken at 16 frames per second frequently show return movement beginning in the second frame after cover is removed, and often completed except for stabilization within one or two more frames.

A word of caution should be added as to recognition of true torsional rotations: In the presence of simultaneous horizontal and vertical rotations, it is easy to mistake normal wheeling movement or "false torsion" for actual torsion, and vice versa. The simplest way to avoid mistakes of this sort is to concentrate attention only on iris or scleral markings which lie in the common plane of the fixating and deviated axes of that eye (for example, in the plane defined by the primary visual line and the visual line of the eye in its dissociated

position, for alternate fixation in the primary direction).

In cases of double hypertropia where the patient is old enough to co-operate, examination with a major amblyoscope yields pertinent information. Brightly illuminated target(s) and very bright, diffuse outside illumination, with observation of the patient's eyes through a magnifying loupe, are desirable. Iris details and small scleral vessels need be clear and prominent to the observer, and should be closely watched while fixation is made to alternate. In this manner, any "objective" changes in the torsional positions of the patient's eye(s) readily become apparent.

A target designed to govern the direction of fixation of an eye toward its center may consist of a dot, a circle or a broken circle of any size, a cross of any size, a short line segment (vertical, horizontal, or oblique), any combination of these, a more intricate design of any size which is sufficiently symmetrical about a clearly apparent center, or any design of sufficiently small size that symmetry makes no appreciable difference. The positions of any two such directional targets, be they similar or dissimilar, can readily be adjusted in a major amblyoscope so as to correspond to any horizontal and/or vertical deviation of the two visual axes. Similar or partially similar targets (unless composed wholly of a central dot, a circle and/or a family of concentric circles) can be adjusted as desired into equivalent or specifically deviated torsional positions. Now the positions of any two directional targets during examination can be adjusted, while alternately illuminating the right target and then the left target, such that a typical case of double hypertropia exhibits the following:

1. With the right target in the primary direction, the left target can be elevated and set horizontally into such a position that during each change in fixation from right eye to left eye (that is, from illumina-

tion of the right target alone to illumination of the left target alone), the *left eye* will not rotate vertically or horizontally (on the average*) as it assumes the fixating role. *The left eye will still intort* during each such change, however. The right eye, during this same change, will extort and rotate vertically away from its original (primary) fixating position, into a position of elevation still higher than that of the now fixating left eye. When illumination is shifted back to the right target instead of the left, the right eye will intort and move back down into its original fixating position, while the left eye will simply extort back into its original dissociated position without moving vertically or horizontally. The average movements accompanying alternation of fixation do not appear to change, qualitatively or quantitatively, when various targets are used, be they similar or dissimilar. Furthermore, when the targets are of such shape as to define torsional orientation (for example, if each target is a simple cross), no change in the torsional position of either target will effect any alteration in the rotations which accompany alternate fixation. (This was puzzling to us when we first began to pay attention to the extorsion accompanying upward rotation of an eye as it dissociated, and the intorsion accompanying downward rotation as it fixated. At that time it seemed logical, without inquiring into the logic involved, that, if a target such as a cross were positioned to correspond horizontally, vertically, and torsionally to the deviated position of the dissociated left eye, and then the left eye instead of the right eye was made to fixate, that the left eye should *not* intort during the change in fixation—but it always did, and the cross was simply visualized as being “tilted”

extorsionally, as it actually was.)

2. Instead, the targets can be moved into such positions that there is no vertical or horizontal jump (on the average) of the *right eye* as fixation is made to alternate. Now, when fixation is shifted from left eye to right eye, the right eye simply intorts, while the left eye extorts and rotates upward to a position higher than that of the right eye. As fixation is made to shift back to the left eye, it rotates back downward and intorts into its original (primary) fixating position, while the right eye simply extorts into its initial dissociated position (this, in turn, of course having been a position of elevation relative to the “primary” position). Again, these movements are not altered by changing the torsional position of either target, or by using different types of targets.

3. When partially dissimilar targets are set as for (1) or (2) and both are illuminated, they cannot be fused, regardless of how the illumination of the separate targets is varied. This holds true even in cases where there usually is bifixation during ordinary life. Indeed, fusion appears impossible unless the targets not only are in quite precisely equivalent torsional positions (if there is any torsionally oriented pattern common to the two targets), but are not separated vertically or horizontally by angles of deviation as great as those normally permissible. Thus, in cases of double hypertropia the ranges of vergence powers for fusion are in general actually smaller than the average normal, and stereopsis is very likely to be faulty.

4. We have never been able to elicit simultaneous macular perception of targets set as for (1) or (2), even if bifixation usually was present during ordinary life.

While the above findings are those of the common, “typical” form of double hypertropia, where alternately dissociated eyes elevate and extort, the same principles appear to hold in the rare instances where there is elevation and intorsion, or depression and intorsion, of the dissoci-

* The qualification “on the average” applies throughout, because there usually is appreciable variation in the deviation of the dissociated eye from second to second, or from one “dissociation” to the next.

ated eye. (Depression with extorsion might also be a rare occurrence, although we have not recognized such a case, and we do not find any described in the literature.)

When we first directed our attention to the torsional deviations associated with double hypertropia, we attempted to measure such deviations by plotting the physiologic blindspots on a stereocampimeter. Of course these attempts were completely unsuccessful, since (as we soon learned) in these cases fixation with an eye simply will not take place while that eye is torsionally deviated from the fixating position of the fellow eye.

We have tried to measure torsional deviation in the older, more co-operative patients by impressing an after-image of a line on the two retinas, while one eye was fixating and the other was dissociated, and asking the patient to draw the apparent positions of the after-image lines during subsequent alternate fixation and/or bifixation. This seemed partially successful in two instances, but even these two patients would only part of the time recognize a dim, broadened after-image line with the previously dissociated eye. This probably was due to the fact that presentation to the dissociated eye of a line stimulus of sufficient intensity to permit recognition of the after-image generally also stimulated at least some partial, wavering movements of that eye toward fixation, and also to the fact that the dissociated eye commonly varies its position somewhat from instant to instant, not infrequently in a somewhat rhythmic although irregular fashion, even though the fixating eye remains steady and the visual stimuli are constant.

We have not tried impressing after-images by means of a high intensity flash, such as with a Strobe tube, which would seem to offer some possibility of producing consistently recognizable after-images of sufficient clarity for worthwhile measurements. As of the present, the only reasonably accurate measurements we have of

the torsional deviations have been obtained by photography.

III. EXPLANATIONS OFFERED FOR DOUBLE HYPERTROPIA

Despite the high incidence and importance of double hypertropia, its pathogenesis and physiologic mechanics have remained an enigma except for a partial visualization of the *modus operandi* in those cases where it is associated with large horizontal deviations.

Fink,⁴ in his recent book on the oblique muscles, says of dissociated vertical divergence, "The cause is unknown. At present the best explanation is a somewhat vague concept of imbalanced innervational activity of the centers controlling vertical movements."

Bielschowsky believed the possible influence of a fusion mechanism was precluded by the fact that it occurred in some cases with so profound an amblyopia of a squinting eye that fusion itself would not be possible. He attributed the deviations to "intermittent and alternating innervations for positive and negative vertical divergence, which are independent of the will and fluctuate in intensity."

Verhoeff believes the ocular motor mechanism is activated differently by different sensory conditions, such that hypothetically he divides it for the purpose of discussion into two monocular conjugate mechanisms, one for each eye, and a binocular conjugate mechanism. Verhoeff says, in effect, that since the disjunctive vertical movements are effected by alternate occlusion and fixation, and since present anatomic and physiologic knowledge require that the conjugate reflex mechanism respond in an equally efficient manner for all voluntary innervation, however derived, that the admittance of visual impulses from the one eye into the sensory association pathways as contrasted with the other, must effect different alterations in the conjugate mechanism. He does not analyze just how these alterations are

effected. He concludes that "occlusion hypertropia" must be due to monocular conjugate excess involving one or both elevators, or to monocular conjugate insufficiency involving one or both depressors, or to both conjugate excess and conjugate insufficiency. He believes the most likely cause to be congenital defects in the conjugate pathways of the superior oblique muscles, and the next most likely a defect in those of the inferior recti.

We propose that the alternate vertical deviations of double hypertropia are merely the vertical components which should be expected, on alternate fixation, from certain underlying, fundamental deviations which have qualitatively "comitant" torsional components. Any deviation should vary according to the position of either eye; and position of the eye must be given in terms of torsional as well as horizontal and vertical components of position. The average resultant of a fundamental deviation which will exhibit the phenomenon of double hypertropia usually has exocyclovergence, and often convergence, as predominant, qualitatively "comitant" component(s). It is not necessary to postulate any fundamental abnormality of the "conjugate pathways," except that the very presence of a deviation does of course indicate these have not become habitually "set" into a precisely normal pattern.

IV. SOME DEFINITIONS, PHYSIOLOGIC BACKGROUND, AND PROBABILITIES

Terminology for describing the rotational positions of the eyes, and their relationships to each other, is not systematic nor always precise. Presentation of the subject at hand unfortunately demands a clearly defined system for describing absolute positions and relative positions of the two eyes; and this is best reduced to symbolic form if it is not to be too cumbersome. It is hoped the system we herewith define, which at first glance will appear formidable because of unfamiliarity, will

soon appear logical and meaningful. We realize the introduction of new, unfamiliar notations will probably necessitate more than one reading of this section, with frequent reference to illustrations to gain familiarity in visualizing what the symbols represent; for this, we apologize.

A. POSITION

The position of an eye will be regarded as its rotational position with respect to an exactly defined primary position, and divisible into horizontal (H), vertical (V), and torsional (T) components. "Torsion" will always indicate rotation about the visual axis, ignoring normal wheeling motions. Exact definition of primary position and of the H, V, and T components of rotation will appear in a later paper.*

* Briefly, the primary position of an eye will be defined anatomically as the position of the globe with respect to the head such that the plane defined by the centers of the two globes and the origins of the medial and lateral recti will also contain the insertions of the horizontal recti (and the visual axis), and the visual axis will be perpendicular to the transverse line joining the centers of the two globes. It is convenient to think of the head as vertically erect, with the defined plane horizontal.

A primary or "orbital" reference frame XYZ-0 will be defined as a right-handed orthogonal system fixed relative to the (right) orbit, with the transverse, anteroposterior (or visual), and vertical axes of the globe (in its primary position) determining the respective positions of X, Y, Z, which will be directed laterally, forward, and upward; and with origin O representing a fixed center of rotation 1.3 mm. behind the center of the globe. A "global" reference frame X'Y'Z'-0 will be regarded as coincident with the orbital reference frame while the eye is in its primary position, but as being fixed in its relationship to the globe and as rotating along with the eye whenever it rotates into some other than its primary position.

For denoting rotational position away from the primary position, H, V, and T can be the respective angles of rotation about the Z, X', and Y' axes, taken in that order, which would rotate the globe from the primary into the specified position. Defined in this manner, T becomes a function of H and V; this is different from 0 for any tertiary position wherein Listing's rule applies. However, in such an instance the value assigned to T represents a false angle of torsion, incident to having defined T as rotation about Y' after Y' has already been rotated about an axis outside the XY plane—that is, about X', which

H, V, and T for either the right or the left eye will be regarded as positive if the eye is rotated to the left, up, or counter-clockwise; negative to the right, down, or clockwise. The convention for signs makes like signs indicate conjugately directed rotations, unlike signs oppositely directed (disjunctive) rotations with respect to the primary positions of the two eyes.

Fixation with an eye means positioning it so a target image falls on the macula and is consciously perceived.

will have been rotated out of the XY plane by the initial horizontal rotation around Z—whereas Listing's rule moves Y' into its final position by rotation about a single (oblique) axis in the XY plane, and hence without rotation around Y. Listing's law does not hold whenever there is any true torsion; here, T, defined as above, represents a combination of false and of true torsion for any tertiary direction of fixation, and hence can be misleading. However, the simple system defined above is perhaps the most easily handled for mathematical computations, and results can readily be transposed into some other system for analysis.

A different way of defining H, V, and T, such that they still define position in terms of angular rotation about Z', X', and Y', but such that the rotational components need not be considered in any particular order, is as follows: Let H be the angle between two planes A and A', where A contains both Z and Z' and where A' bears the same relationship to the X'Y'Z'-0 frame as A does to the XYZ-0 frame. (If Z and Z' coincide, A may be any one of an infinitude of planes. If Z and Z' do not coincide, they still meet at 0 and consequently lie within and define A as a (unique) plane.) Similarly, let V be the angle between planes B and B', where B contains X and X', and where B' is defined with respect to X'Y'Z'-0 exactly as B is defined with respect to XYZ-0. Also similarly, let T be the angle between two planes C and C', where C contains both Y and Y', and where the equation of C' in terms of X'Y'Z'-0 is the same as the equation for plane C in terms of XYZ-0. (Locations of the C planes are indicated by broken lines, and of the C' planes by two heavy dots, in the illustrations in this paper.)

For this paper, we will consider H to be the angle of rotation of the visual line Y' about the Z axis, and V the angle of rotation of Y' about X', taken in that order, such as would point the fixation axis in the specified direction. H and V will thus conform to their measures as taken with a major amblyoscope. However, we will consider T to be the angle between planes C and C', as outlined above, so that values of T different from zero will always represent true torsion.

Dissociation of an eye means exclusion of images from reaching conscious perception by way of that eye. Dissociation may result from suppression, or it may be brought about by covering the eye or otherwise interfering with its image formation.

The right eye (R) or the left eye (L) will be designated as fixating by a dot over its symbol \dot{R} or \dot{L} or by a bold-faced **R** or **L**; dissociated (nonfixating) by a wavy line over \dot{R} or \dot{L} or by an italicized *R* or *L*; or if it is desired not to specify whether it is fixating, simply by R or L. Fixation will be regarded as directed toward a distant target, and with any refractive error corrected, unless otherwise specified.

Position will be designated as R(H, V, T) for the right eye, L(H, V, T) for the left. For example, let us describe the right eye fixating in a position of 10-degree adduction, 15-degree depression, and 10-degree intorsion (fig. 5): it will be turned 10 degrees to the left, 15 degrees down, and 10 degrees clockwise from its primary position; therefore $H = +10^\circ$, $V = -15^\circ$, $T = -10^\circ$; and its position, as well as the fact that it is fixating, is specified by $\dot{R}(+10^\circ, -15^\circ, -10^\circ)$. Conversely, $L(+35^\circ, -15^\circ, -10^\circ)$ indicates (see also Figure 5) the left eye is not fixating, $H = +35^\circ$, $V = -15^\circ$, $T = -10^\circ$; thus it is 35 degrees to the left, 15 degrees down, and 10 degrees clockwise from its primary position; it is therefore 35-degrees abducted, 15-degrees depressed, and 10-degrees extorted; and it is dissociated.

Use of H, V, or T without a subscript will indicate that positional component is not specified—that is, that it may vary. Thus $R(-10^\circ, V, T)$ indicates the right eye is not fixating, is abducted 10 degrees, and its vertical and torsional positions are not specified. A number subscript attached to H, V, or T will indicate the corresponding component represents some unstated but specific angle, which remains constant. Thus, $L(-10^\circ, +V_1, -T_1)$ indicates the

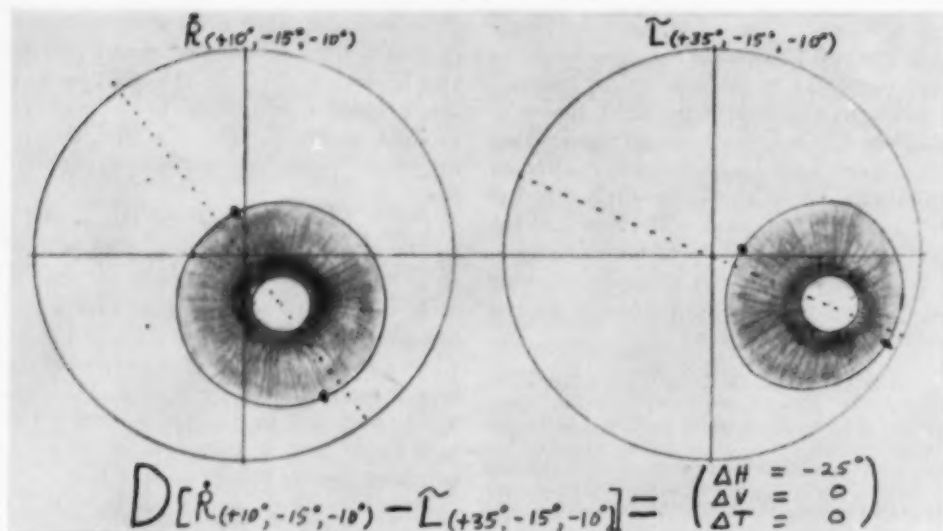


Fig. 5 (Guyton and Kirkman). Symbolic designation of position, and of fixation and dissociation. See text.

left eye may or may not be fixating, is adducted 10 degrees, is elevated by an angle V_1 , and is extorted by an angle T_1 . A small letter subscript such as in $R(H_a, V_a, T_a)$ will indicate any one of all possible arbitrary values for each component so designated.

For the two eyes to be in "equivalent" positions will mean equivalence of all or of specified components, both in degree and in direction. Thus, $R(+5^\circ, -12^\circ, -6^\circ)$ and $L(+5^\circ, -12^\circ, -6^\circ)$ indicate complete equivalence (fig. 6). As an additional example, $R(0, V, T_1)$ and $L(0, V, -T_1)$ indicate equivalent horizontal, nonspecified vertical, and nonequivalent torsional positions, the torsional components being equal in magnitude but opposite in direction.

It should be repeated that the convention for signs makes respective positional components of the two eyes which bear similar signs indicate conjugately directed rotations, unlike signs oppositely directed (disjunctive) rotations, away from their primary positions. For complete equivalence of position, however, the respective

components must not only bear similar signs, but must be equal in magnitudes.

We will abbreviate an arbitrary position $R(H_a, V_a, T_a)$ as simply R_a or $L(H_a + H_b, V_a + V_b, T_a + T_b)$ as L_{a+b} , and so forth. R_a and L_a will thus indicate some arbitrary but completely equivalent position for the two eyes, which will be different from some other equivalent position R_b and L_b , and so forth.

The primary position of an eye will be $R(0, 0, 0)$ or $L(0, 0, 0)$. However, fixation of the right eye in the primary direction of gaze properly should be designated as $R(0, 0, T_0)$, since fixation in the primary direction does not necessarily make the torsional position of the eye correspond to the anatomically defined torsional position (where the midpoints of the insertions of the medial and horizontal recti lie in the primary horizontal plane). Nevertheless, for reasons given later, we will (somewhat improperly) designate fixation in the primary direction the same as fixation in the primary position, abbreviated as R_0 , or L_0 .

The positions of physiologic rest will be designated as RL . These positions will be

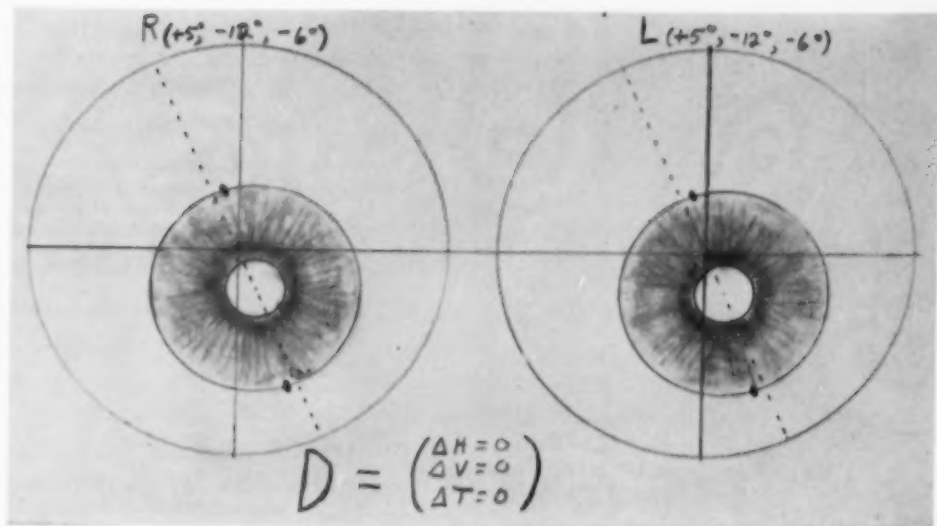


Fig. 6 (Guyton and Kirkman). Complete equivalence of position of the two eyes.

regarded as those assumed by the two eyes when the sum of all the extraocular muscle tensions (the passive elastic tension plus the active neurogenic tension from tonic stimulation, summated for all extraocular muscles) is a minimum—that is, when the head is symmetrically erect and immobile, the eyes are normally open, there is complete darkness and quiet so there are no visual, auditory or other external stimuli, and there is no utilization of voluntary stimulation for controlling the eyes.

B. DEVIATION

Thus far, we have dealt with positions of the eyes defined with respect to their (anatomic) primary position. Practically, we are more concerned with any differences in the positions of the two eyes, as related to each other.

We will call a difference in position of the two eyes a *deviation*, and represent

this difference by $D = \begin{pmatrix} \Delta H \\ \Delta V \\ \Delta T \end{pmatrix}$ to express

it as differences in the respective rotational components. We will adopt the convention of always subtracting $L(H, V, T)$ from

$$R(H, V, T) \text{ to obtain } D[R - L] = \begin{pmatrix} \Delta H \\ \Delta V \\ \Delta T \end{pmatrix},$$

regardless of which eye is fixating. This will serve to make the signs of the component deviations indicate their sense: now, $+\Delta H$ indicates horizontal convergence, $-\Delta H$ horizontal divergence; $+\Delta V$ means the right eye is elevated with respect to the left (so the left eye is depressed with respect to the right), $-\Delta V$ indicates the left eye is elevated with respect to the right (and the right eye is depressed with respect to the left); $+\Delta T$ indicates excyclovergence, $-\Delta T$ means incyclovergence.

For example (fig. 7), the difference in position of $R(-20^\circ, -5^\circ, -6^\circ)$ and $L(15^\circ, -2^\circ, 1^\circ)$ may be expressed as

$$D[R(-20^\circ, -5^\circ, -6^\circ) - L(15^\circ, -2^\circ, 1^\circ)] = \begin{pmatrix} \Delta H = -35^\circ \\ \Delta V = -3^\circ \\ \Delta T = -7^\circ \end{pmatrix}.$$

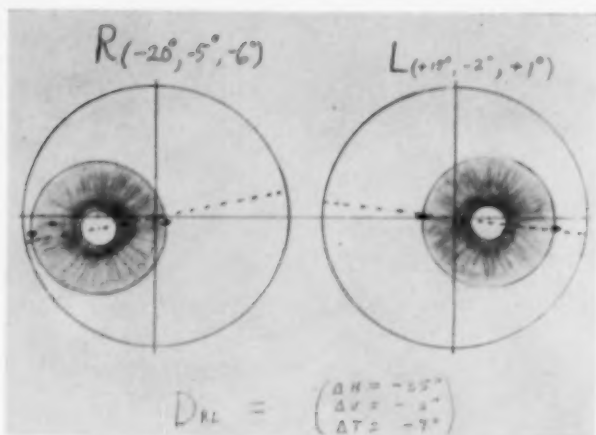


Fig. 7 (Guyton and Kirkman). Deviation of two eyes whose positions are given in terms of rotational components. See text.

This means there is 35° exo-, 3° left hyper-, and 7° incyclo.

Let us take Figure 5 as a second example:

$$D[R(10^\circ, -15^\circ, -10^\circ) \\ -L(35^\circ, -15^\circ, -10^\circ)] = \begin{bmatrix} \Delta H = -25^\circ \\ \Delta V = 0 \\ \Delta T = 0 \end{bmatrix}$$

This means there is 25-degrees horizontal divergence, vertical equivalence, and torsional equivalence.

C. VARIATION IN DEVIATIONS ON ALTERNATE FIXATION: COMPOSITE REPRESENTATION

1. Alternate fixation in the primary direction.

The vertical component of deviation differs in double hypertropia according to which eye is fixating. Also, in certain cases there is a significant difference in the horizontal component and/or the torsional component. We will find it convenient to represent the differing deviational components for alternate fixation in a composite form.

We will use the abbreviation **RL** to indicate the right eye is fixating in the primary direction while the left eye is dissociated; and **RL** to indicate the right eye

is dissociated and the left eye is fixating in the primary direction. We will let

$$D_{RL} = \begin{bmatrix} \Delta H_{RL} \\ \Delta V_{RL} \\ \Delta T_{RL} \end{bmatrix} \quad \text{and} \quad D_{RL} = \begin{bmatrix} \Delta H_{RL} \\ \Delta V_{RL} \\ \Delta T_{RL} \end{bmatrix}$$

indicate the respective deviations.

The average horizontal component $\overline{\Delta H}$ will be $\frac{\Delta H_{RL} + \Delta H_{RL}}{2}$. Also, $\frac{\Delta H_{RL} - \Delta H_{RL}}{2}$

will give an "alternating" factor $\overleftrightarrow{\Delta H}$ which represents the variation in ΔH due to the effects of alternate fixation, and which will need be added to $\overline{\Delta H}$ to give ΔH_{RL} , or be subtracted from $\overline{\Delta H}$ to give ΔH_{RL} .

Similarly,

$$\overline{\Delta V} = \frac{\Delta V_{RL} + \Delta V_{RL}}{2}, \quad \text{and}$$

$$\overleftrightarrow{\Delta V} = \frac{\Delta V_{RL} - \Delta V_{RL}}{2};$$

$$\overline{\Delta T} = \frac{\Delta T_{RL} + \Delta T_{RL}}{2}, \quad \text{and}$$

$$\overleftrightarrow{\Delta T} = \frac{\Delta T_{RL} - \Delta T_{RL}}{2}.$$

Note that in each instance the component for *RL* is subtracted from the respective component for *RL* in determining the "alternating" factor $\Delta(\overleftrightarrow{\quad})$. This convention determines the sign of $\Delta(\overleftrightarrow{\quad})$. If we represent the composite horizontal component of deviation as $\Delta H_{RL}^{\overleftrightarrow{RL}} = \overline{\Delta H} \pm \Delta H$, the sign of ΔH can be incorporated into the \pm preceding it, leaving it \pm if ΔH is positive, and making it \mp if ΔH is negative. Thus, $\overline{\Delta H}$ is the average, ΔH with the top sign attached is the amount to be added for the situation *RL*, and ΔH with the lower sign attached is the amount to be added to portray the situation *RL*.

We can now express the composite deviations as follows:

$$D_{RL}^{\overleftrightarrow{RL}} = \begin{pmatrix} \overline{\Delta H} \pm \Delta H \\ \overline{\Delta V} \pm \Delta V \\ \overline{\Delta T} \pm \Delta T \end{pmatrix}.$$

For example, consider the situation where the positions of the eyes on alternate primary fixation are *R*(0, 0, 0) *L*(-20°, +7°, -6°) and *R*(+16°, +9°, +10°) *L*(0, 0, 0). (fig. 8). We see that

$$D_{RL} = \begin{pmatrix} \Delta H = +20^\circ \\ \Delta V = -7^\circ \\ \Delta T = +6^\circ \end{pmatrix} \quad \text{and} \quad D_{RL} = \begin{pmatrix} \Delta H = +16^\circ \\ \Delta V = +9^\circ \\ \Delta T = +10^\circ \end{pmatrix}.$$

Putting these together,

$$D_{RL}^{\overleftrightarrow{RL}} = \begin{pmatrix} \overline{\Delta H} = +18^\circ, \overleftrightarrow{\Delta H} = \pm 2^\circ \\ \overline{\Delta V} = +1^\circ, \overleftrightarrow{\Delta V} = \mp 8^\circ \\ \overline{\Delta T} = +8^\circ, \overleftrightarrow{\Delta T} = \mp 2^\circ \end{pmatrix}.$$

Interpreting this,

(1) $\overline{\Delta H} = +18^\circ$, $\overleftrightarrow{\Delta H} \pm 2$ means an average

eso- of 18 is increased by 2 for *RL* and decreased by 2 for *RL*.

(2) $\overline{\Delta V} = +1^\circ$, $\overleftrightarrow{\Delta V} = \mp 8$ means an average right hyper- of 1 is decreased by 8 for *RL* and increased by 8 for *RL*.

(3) $\overline{\Delta T} = +8^\circ$, $\overleftrightarrow{\Delta T} = \mp 2$ means an excyclo- of 8 is decreased by 2 for *RL* and increased by 2 for *RL*.

For other examples, refer back to Figure 1, and see Figure 9A.

2. Alternate fixation in directions compensating for ΔH and ΔV , symmetric to the primary direction.

Instead, let us measure the component deviations, during alternate fixation, while the horizontal component ΔH and the vertical component ΔV are symmetrically compensated for, and hence measured. To indicate this has been done, we will use symbols \sim and $\overleftrightarrow{\quad}$ instead of $-$ and $+$ to designate the average and the alternating components.

For the actual measurements we may use alternate cover, with equal horizontal and equal vertical prisms of appropriate strength before the two eyes and a target in the primary direction; or we may employ a major amblyoscope, alternately illuminating the targets while the arms are placed to correct symmetrically for ΔH and ΔV . The alternate deviations may be represented in the composite form:

$$D_{RL}^{\overleftrightarrow{RL}} = \begin{pmatrix} \overline{\Delta H} \pm \Delta H \\ \overline{\Delta V} \pm \Delta V \\ \overline{\Delta T} \pm \Delta T \end{pmatrix}, \text{ where}$$

ΔH is calculated similarly to $\overline{\Delta H}$, ΔH similarly to $\overleftrightarrow{\Delta H}$, etc.

A numerical example is given in Figure 9B, for the same case portrayed in Figure 9A. When $\overline{\Delta H}$ is large, $\overleftrightarrow{\Delta V}$ may depend on both $\overline{\Delta T}$ and $\overleftrightarrow{\Delta H}$, whereas ΔV will depend on ΔT alone (see later). In other respects, the two sets of measurements are generally

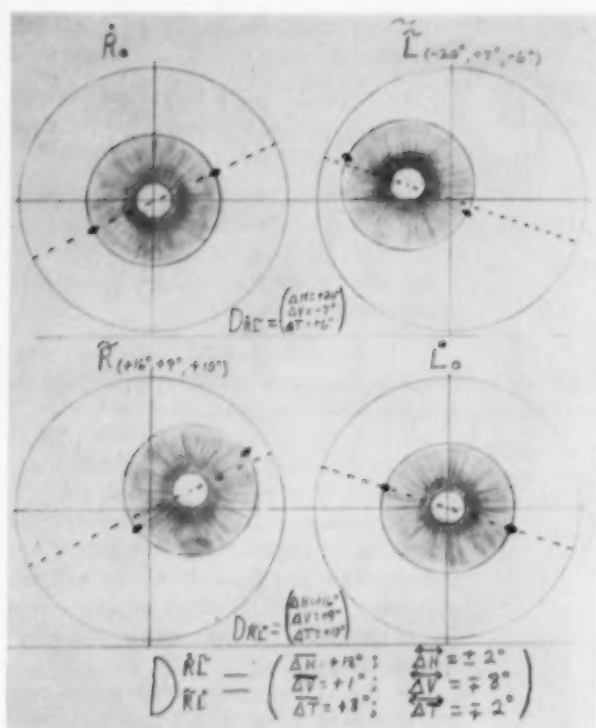


Fig. 8 (Guyton and Kirkman). Composite representation of deviations for alternate fixation in the primary direction.

nearly the same, as is evident from comparing Figure 9A with Figure 9B.

It should be mentioned that a deviation in the positions of physiologic rest of the two eyes cannot readily be measured, but the components of the "rest deviation" are approached by ΔH , ΔV , and ΔT (or by $\hat{\Delta H}$, $\hat{\Delta V}$, and $\hat{\Delta T}$, since these are almost the same).

3. *Alternate fixation in directions compensating for ΔH and ΔV , symmetric to $H = +30^\circ$ or $H = -30^\circ$.*

Similarly, measurements may be made for fixation symmetric around the 30 degrees eyes left ($H = +30^\circ$) or the 30 degrees eyes right ($H = -30^\circ$) directions. The signs $\hat{\Delta}$ and $\hat{\Delta}$ or $\hat{\Delta}$ and $\hat{\Delta}$ will be used above the average and the alternating compo-

nents for these respective directions, in a manner entirely analogous to that above.

We actually will only want to know how much $\hat{\Delta V}$ and $\hat{\Delta V}$ differ, respectively, from $\hat{\Delta V}$. Practical difficulties in obtaining even these measures decrease their dependability, and hence their usefulness, to a considerable extent. However, Figures 9C and 9D portray all the components of these deviations, for the same case illustrated in Figures 9A and 9B—this case will be used later as an example for planning the surgical corrections.

The particular directions $H = +30^\circ$ and $H = -30^\circ$ are chosen for measuring variations from $\hat{\Delta V}$ because in these directions the relative effectiveness of the obliques and the vertical recti as vertical elevators

Fig. 9A (Guyton and Kirkman). Alternating hypertropia. Alternate fixation in the primary direction.

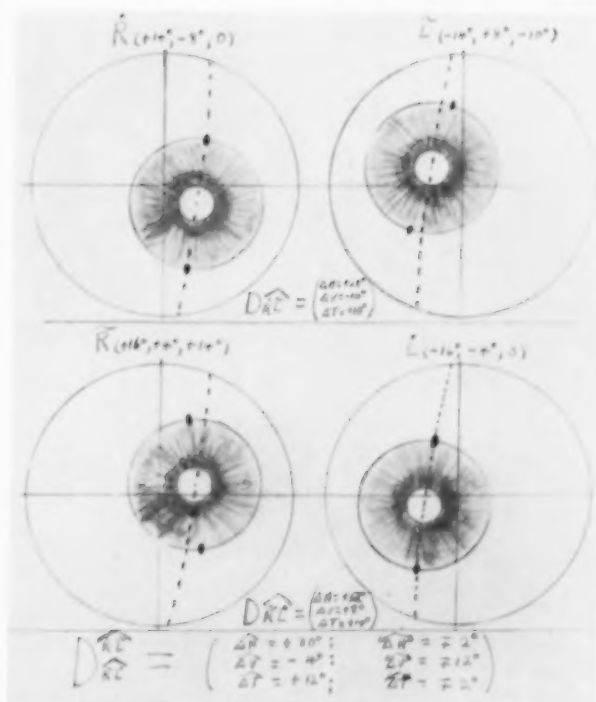
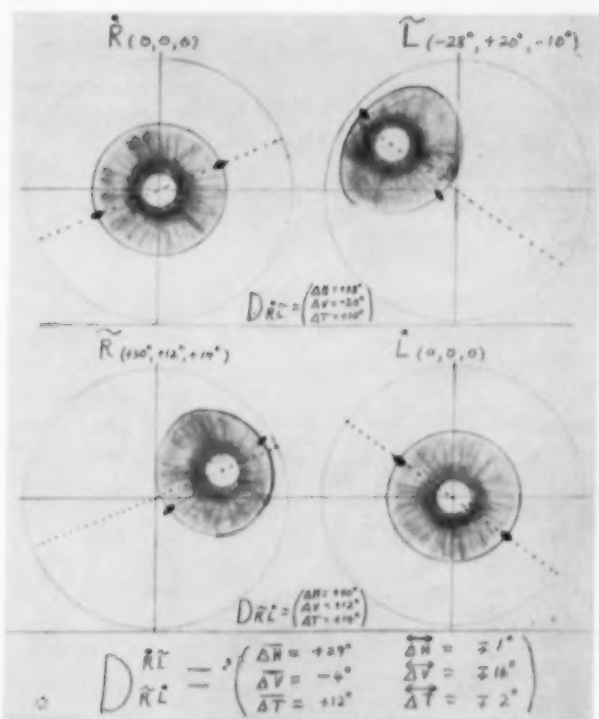


Fig. 9B (Guyton and Kirkman). Alternating hypertropia. Same case as in Figure 9A. Alternate fixation in directions compensating for ΔH and ΔV , symmetric to the primary direction.

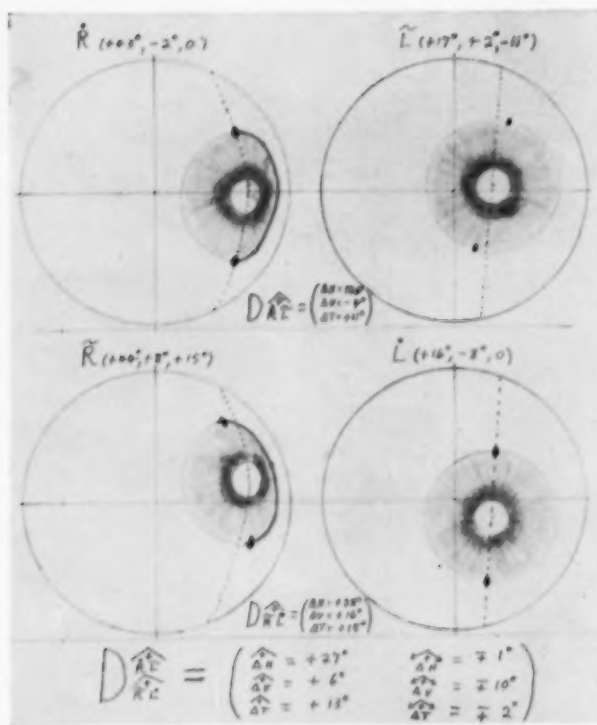
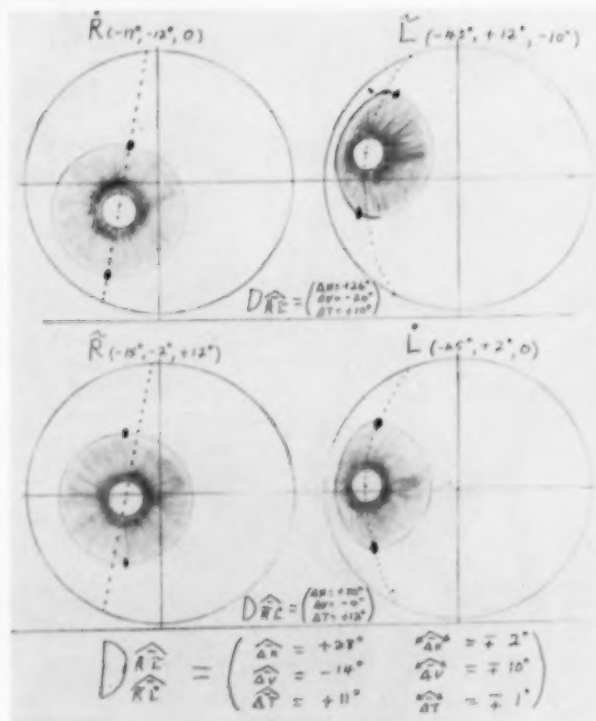


Fig. 9C (Guyton and Kirkman). Alternating hypertropia. Same case as in Figures 9A and 9B. Alternate fixation in directions symmetric to $H = +30$ degrees.

Fig. 9D (Guyton and Kirkman). Alternating hypertropia. Same case as in Figures 9A, 9B, and 9C. Alternate fixation in directions symmetric to $H = -30$ degrees.



becomes (approximately) either halved or doubled, as the case may be.*

D. CONJUGATE AND FUSIONAL STIMULI, FIXATION AND SUPPRESSION

It is convenient to divide higher order motor stimuli which maintain or change the positions of the eyes into two main groups, conjugate and fusional. Primitive conjugate stimuli stem from postural, vestibular, auditory and protective reflexes. Conjugate stimuli of cortical level derive from the involuntary fixation reflex, and from voluntary direction of fixation. Fusional stimuli are of cortical level, arising from reflex efforts to bring the visual afferent stimuli from the two eyes into corresponding patterns, so they can be correlated homogeneously with other sensory stimuli. Development of the accommodation-convergence reflex association is controlled by fusional stimuli, and may be regarded as a lower order accessory of the fusion reflex.

Normally, the fusion reflexes modulate motor stimulation to effect bifixation. During the course of time, modulation of the lower motor patterns by fusional stimuli

facilitate or inhibit various of the synaptic connections into such an habitually set form that rotations of the eyes become almost exactly synchronous even when one or both eyes are prevented from receiving visual stimuli. However, when one or both eyes are covered, some small but measurable asynchrony of movement is normal at the extreme limits of physiologic rotations; there are imperfections in horizontal alignment, reflecting the effect of varying convergence during bifixation at different distances; and there often are much smaller imperfections in vertical or torsional alignment.

Fusional stimuli, including those for convergence, continue to influence the motor reflex pattern for conjugate movement throughout life. However, as the lower motor pattern becomes increasingly "set" with age, an increasing degree of neural activity is required for fusional stimuli to alter the "set" pattern beyond its habitual limits of normal variation. "Conjugate" stimuli, on the other hand, whether of cortical or lower level origin, traverse the "set" lower motor pattern with relative ease, causing ocular rotations *via*, and strictly in keeping with, the "set" of that particular pattern.

Conjugate stimuli are taken to mean stimuli, devoid of fusional modifications, which tend to control the positions and movements of both the eyes together. A precisely functioning conjugate mechanism is taken to mean an habitually "set" pattern of synapses which will correlate conjugate stimuli with proprioceptive stimuli and so modify the former, for relay to the separate eyes, that a change in conjugate stimulation which would move the right eye from any position R_a to any other position R_b would also move the left eye from L_a to L_b .

To speak of a "precisely functioning conjugate mechanism" in the presence of a deviation is something of an absurdity, because a precisely functioning conjugate mechanism should demand the positions of

* This approximation is based on data which will appear in a later paper. This data, which allows for "fouling" of the IO and IR, and partial "locking" of their connective tissue sheaths, indicates the following "momentages" available for vertical rotation of the right eye:

	H = -30°	H = 0°	H = +30°
SO	-0.37	-0.66	-0.90
IO	+0.45	+0.72	+0.87
SR	+1.00	+0.87	+0.58
IR	-0.97	-0.88	-0.57
SO + IO	0.82	1.38	1.77
SR + IR	1.97	1.75	1.15
obl./v. recti	0.41	0.79	1.54

Krewson's⁸ calculations, while yielding nearly the same total ratios for these positions (0.40, 0.74, and 1.53), are actually far different: they indicate a *decreasing* effectiveness of the IO during inward rotation, with a steeply *increasing* effectiveness of the SO.

the two eyes be maintained in positions of complete equivalence except when its functioning is modified by fusional (including accommodative) stimuli. However, in a purely imaginary sense, it can be considered precise if it *should* serve to maintain equivalence on movement *if* the eyes were in initially equivalent positions. It is so used in this paper.

The primitive reflex pathways inherent in a newborn baby result in imperfectly conjugate movements of the eyes. This can be demonstrated by holding a very young baby in an upright position and tilting him (fairly rapidly) first to the right and then to the left: as his head tilts to the right, the right eye intorts and the left eye extorts, but also there generally is an associated downward rotation of the right eye and upward rotation of the left eye; the converse applies on tilting him to the left.

Exact synchronization of position or of movement will not develop if one eye is blind from birth. Also, conjugate movements may gradually become less precise if an eye is blinded. Such loss of precision varies more or less inversely as the age at which the eye was blinded, and directly as the subsequent elapse of time.

If the conjugate mechanism is not precise in its "set," the required change in conjugate stimulation for moving the right eye from position R_a to R_b may be different than that for moving the left eye from L_a to L_b . However, any given change in conjugate stimulation should still result only in unequal, never oppositely directed components of rotation of the two eyes if each started from the same position. Erroneous extrapolation to include situations where the two eyes do *not* start from the same positions has been one of the major reasons double hypertropia has appeared paradoxical.

If visual stimuli provide insufficient reflex modulation of the motor patterns to maintain bifixation, the visual impulses from one eye (at a time) become largely inhibited from reaching the interpretative

sensorium, while those from the other eye are facilitated. In such an event, there then develops habitual or intermittent monocular fixation, which may be either alternate or almost unilateral. The qualification "almost" is necessary because there are always times during everyday life, however transient, when a usually fixating eye is covered or obscured to the extent that visual impulses from the other eye partially break through the inhibitional barrier.

Usually the nonfixating eye is suppressed to the point it does not interfere with the interpretation of detail, which means relatively great central suppression but progressively less peripheral suppression. However, even in cases of unilateral suppression with habitually profound amblyopia, the amblyopic eye generally will make an attempt at fixation when the other eye is covered, and will at least attempt to align meridional contours. Indeed, even with the normally fixating eye uncovered, an effect of fixation stimuli on the amblyopic eye is often seen in the form of variable and incomplete movements toward the bifixation position, as will be described when we interpret the Bielschowsky phenomenon; and these movements in time often become rhythmical, representing habituation of low-order feed-back reflex circuits.

E. PATHOGENIC PROBABILITIES

Considerations which are based on the fact that the neuromuscular and fibrous attachments of the eyes develop and function in conformity to principles applicable throughout the remainder of the body lead to certain probabilities. While these probabilities may in part smack of rank heresy to some ophthalmologists, they nevertheless must be regarded as tentatively correct unless they can be proved otherwise, and we know of no acceptable proof to their contrary. They are as follows:

1. Congenital paresis of an extraocular muscle, either a congenital deficiency of

contractile elements or of motor nerve fibers, should not occur with substantially higher frequency than congenital paresis of the levator or other striate muscles. It should in fact be so uncommon as not to constitute a significant factor in the pathogenesis of squints.

2. Congenital defects of the higher neurones involved in the development of normal synaptic patterns for fixation, bifixation, and conjugate movements should also be rare.

However, abnormal synaptic patterns may well develop from abnormal utilization of anatomically correct pathways. The neurogenic effort available for overcoming obstacles to the development and maintenance of bifixation (and a normally precise conjugate mechanism) should vary somewhat from individual to individual, and from time to time in the same individual. If obstacles to bifixation demand neural activity so large and variable as to exceed the available "neurogenic effort," the abnormal pattern which develops (for monocular fixation) should be the one which is physiologically most advantageous, and requires the least neural activity, for that situation. Obstacles to bifixation should be expected from any combination of: (a) unequal or deficient retinal image(s), (b) excessive utilization of accommodation-convergence association from hyperopia, and vice versa, (c) anatomic variation in the sites of muscle origins and insertions, (d) anatomic variation in connective tissue attachments of the globes. The last two will be discussed briefly.

3. While the origins and insertions of the rectus muscles are anatomically nearly constant and are rather uniformly symmetrical, those of the obliques vary considerably in their anatomic relationships and normally are very appreciably asymmetrical. Indeed, the average normal "line of action" of a superior oblique is sufficiently asymmetrical with respect to that of the inferior oblique* to require comparatively large changes in the individual stim-

ulations of the various muscles to maintain equivalence in positions of the two eyes for differing fixating directions. Variation beyond the average normal may often be a major factor in demanding a degree of neural activity, for complete maintenance of equivalence, which exceeds the "neurogenic effort" required for suppression, instead.

4. "Congenital adhesions" of muscles, tendons or sheaths to each other or to the globe, or "congenital fibrosis" of muscles, should likewise be rare. Indeed, the relatively strong and inflexible connections often described later on as "congenital adhesions," or the comparative rigidity of muscle frameworks so often ascribed in later life to "congenital fibrosis," are practically nonexistent within the first few months of life. These characteristics develop physiologically (and progressively) in any fibrillar tissue which is subjected to less than its average normal range of extension during everyday life.

However, there is considerable "normal" variation in the initial proportion of connective tissue in any given location, and a more than average amount of this poor biologic elastomer can render normally full extensions more difficult; and progressive "contracture" will occur if counterbalancing stretching forces are insufficient.† If bifixation is not maintained, there are slight limitations in the customary ranges of ocular rotations, and these become more marked over long periods of time.

V. THEOREM I: TORSIONAL EQUIVALENCE ON ALTERNATIVE FIXATION

A. THEOREM I

Fixation of an eye on a target, either binocularly or with either eye separately, demands the fixating positions of the two globes (relative to any given postural posi-

* Numerical values will be given in another paper.

† This subject will be dealt with in detail in a subsequent paper.

tion of the head) must be exactly equivalent, in all three rotational components, for proper (subjectively equivalent) spatial orientation: that is, not only must the horizontal and vertical rotational components of each eye be such as to point the visual axes in equivalent directions toward the target, but also the torsional components of rotational position must be such as to place corresponding retinal meridians into equivalent positions.

Symbolically, Theorem I merely states that if spatial orientation is subjectively the same with either eye fixating,

$$\mathbf{R}(H_a, V_a, T) = \mathbf{R}(H_a, V_a, T_a)$$

and

$$\mathbf{L}(H_a, V_a, T) = \mathbf{L}(H_a, V_a, T_a)$$

$$a = 1, 2, 3, \dots, n$$

B. PROOF

Anatomically preset final common pathways demand anatomically precise correspondence of retinal meridians (for example, the meridians which delimit decussation). They do so even more surely than they determine that the lines of vision for fixation shall be foveal. There may exist an "abnormal retinal correspondence" such that foveal fixation with one eye corresponds to a vaguely delimited, always somewhat variable area of retina outside the completely suppressed foveal region of the other eye. However, even such an eye will attempt to align itself meridionally with respect to the other eye in response to stimuli containing oblique, vertical, or horizontal contours. For it to do otherwise, while any appreciable proportion of its peripheral image stimuli are being partially correlated in the interpretative sensorium, would involve such complex multiplication of synapses as to be cybernetically improbable.

C. INTERPRETATIONS

Note that this theorem does not require

the anatomically horizontal meridians of the retinas actually to be horizontal (with the head vertically erect) for any direction of fixation, but only to be in equivalent torsional positions. Thus fixation in the primary direction requires only that $\mathbf{R}(0, 0, T) = \mathbf{R}(0, 0, T_0)$ and $\mathbf{L}(0, 0, T) = \mathbf{L}(0, 0, T_0)$, where T_0 always represents the same angle for that pair of eyes. There is no reason for T_0 to be exactly 0 except for symmetry, and slight asymmetry is very common. Also, for some other fixating position $\mathbf{R}(H_a, V_a, T_a)$, Theorem I does not require T_a to be exactly the same as T_0 . However, neither T_0 nor T_a are likely to deviate very far from 0, because very large degrees of asymmetry (of the face, muscle origins or insertions, size of globes, and so forth) are uncommon; and T_a remains very close to T_0 over large ranges of H and V . Thus while Theorem I would not be strictly applicable to the situation

$\mathbf{D}_{RL}^{\mathbf{RL}}$, from a practical standpoint it still holds true for fixation in the different directions required.

It is notable that Donders⁵ in 1847 promulgated the following law: "For any determinate position of the line of fixation with respect to the head, thereto corresponds a determinate and invariable angle of torsion, a value independent of the observer, independent also of the manner in which the line of fixation has been brought into the considered position." The "torsion" of Donders is the false torsion explained in the footnote on page 446, and Donders' law in our notations actually means that T must always be 0. While this law subsequently has been shown not always to hold, its very promulgation is indicative of how close T normally remains to 0.

Theorem I requires torsional equivalence of corresponding fixating positions if there is subjective equivalence of spatial orientation, but it does not require torsional equivalence if images seen with one eye are subjectively tilted—to the con-

trary, in such cases the fixating position of one eye must be torsionally deviated from that of the other for equivalent directions of fixation. The following case is instructive:

A man had had apparently normal binocular vision until the age of 13 years, when he developed a dense corneal leukoma of one eye. This never cleared to beyond 8/200 vision. At about the age of 25 years the faint image seen with that eye began to appear slightly tilted, and this gradually increased in degree. At the age of 48, a corneal transplant gave that eye 20/30 vision (corrected). It also gave him a most annoying torsional diplopia. Torsional deviation measured 20 degrees. Two operations reduced this, but not to the point he could fuse. At the age of 58 years, the image seen with that eye still appeared tilted 10 degrees out of proper position, though he had learned to ignore it such that diplopia was not very bothersome. The torsional deviation measured with a major amblyoscope, either with both eyes fixating or one at a time (that is, by setting lines subjectively horizontal or vertical), was 10 degrees. It measured the same on after-image test. Also on mapping the respective physiologic blindspots with the head rigidly fixed in the same position, that of the faulty eye was extorted 10 degrees from its normal position. Alternate occlusion was not accompanied by any torsional movements. He was not willing to have his good eye occluded long enough to see whether his torsional orientation would readjust to conform with that of his bad eye: in a trial of several hours, he could tell no change.

The diplopia in the above case may be likened to that of any squint acquired after normal binocular vision is firmly established.

Theorem I also does not prohibit there being a small amount of torsional phoria, which is annulled by fusional stimuli in ordinary life, from becoming evident when measured with nonfusional targets (for example, parallel horizontal lines) on a major amblyoscope. In such cases, however, when each eye is made to fix separately, one after the other, there still is a subjectively apparent tilt with the less dominant eye, or occasionally oppositely directed apparent tilting of each of the two images from the subjectively imagined true horizon, if there is no clear-cut dominance of either eye. Such patients do not have an ability to suppress, bifixation having developed normally.

In cases of intermittent or constant

tropia, where there is ability to suppress, a subjective "tilt" cannot be elicited either on monocular or binocular fixation. Apparently, after acquisition of such an ability to suppress, the image from a fixating eye must be in that rather precise torsional position as to give information which is correctly oriented (torsionally) for that sensorium. Since the act of fixation with such an eye causes it to move into proper torsional position, and the fixation reflex is of cortical level, it seems that "suppression" probably takes place somewhere in the sensory correlation pathways between first order neurones of the occipital cortex and higher neurones of conscious visual interpretation.

In bifixation, disparity in meridional positions, without diplopia, is limited to a very small range. This range is less for horizontal contours than for vertical, for narrow than for broad lines, for long than for short lines. Yet the existence of a small range of permissible disparity in bifixation, without abnormal orientation, may possibly be utilized to its maximum extent in certain cases of intermittent excyclovergent tropia where there is only second-grade fusion: lack of stereopsis could possibly be accounted for on this basis. In such cases, covering one eye should cause the still fixating eye to intort (very slightly) into a more exact meridional position, such that the sensory interpretation of orientation would be the same for the monocular image as for the partially fused, but torsionally very slightly disparate images during bifixation.

Thus, with alternate fixation and suppression there develops a reflex whereby visual stimuli are facilitated when and only when the eye is properly (equivalently) positioned, both directionally and meridionally, with respect to posture and to the spatial pattern receiving attention. Conversely, when attention is directed consciously or involuntarily to stimuli entering such an eye, that eye is reflexly directed into the habitually proper position, tor-

sional included, for correct orientation.

This fact will be used in explaining double hypertropia, and it should be noted that ability to suppress one or alternate eyes is prerequisite to exact equivalence being demanded with alternate fixation.

Otherwise, fixation may occur in torsionally deviated positions, which will simply be recognized as such subjectively. In cases of the latter type, where a cyclophoria is apparent on artificial dissociation, the conjugate mechanism has apparently functioned precisely under the influence of fusional stimuli during everyday life, at least during the early years of life while fixation habits were becoming established, such that suppression has not developed. A gradual increase in the tendency to torsional deviation such as to surpass the amount which fusional stimuli will overcome should then result in torsional diplopia, unless one or alternate images be suppressed.*

VI. THEOREM II: NONCOMITANCE OF ALL SQUINTS

A. THEOREM II

A change in conjugately applied motor stimulation which will move the right eye from an initial position R_a into position R_{a+b} should *not* move the left eye from a different initial position L_a *exactly* into position L_{a+b} , even if there should happen to be a precisely functioning conjugate

mechanism. This should still hold true if the initial position of the left eye is equivalent to the final position of the right eye: thus if R_a moves to R_{a+b} , then L_{a+b} should *not* move exactly to L_{a+2b} , but rather to L_{a+b+d} , where d is not exactly the same as b for any individual component. In this case, where the initial deviation of the two eyes is

$$D[R_a - L_{a+b}] = \begin{bmatrix} \Delta H = -H_b \\ \Delta V = -V_b \\ \Delta T = -T_b \end{bmatrix},$$

the deviation after the change in the pattern of conjugate stimuli should be

$$D[R_{a+b} - L_{a+b+d}] = \begin{bmatrix} \Delta H = -H_d \\ \Delta V = -V_d \\ \Delta T = -T_d \end{bmatrix},$$

each component being different.

B. PROOF

For the condition that there be a "precisely functioning conjugate mechanism," we need to show that a *change* in the final motor stimulation pattern reaching the extraocular muscles of the right eye which will move it from R_a to R_{a+b} would *not* move it from R_{a+b} exactly to R_{a+2b} , and (in more general form) would not move it from R_c (where $c \neq a$) exactly to R_{c+b} ; and furthermore, that the change in each rotational component of position will be different if the eye starts out at position R_c than if it started out at position R_a . Such proof will also cover the situation where the conjugate mechanism is not precise, since the latter would only introduce another variable function different from, and without reason to counter-balance, the effects of those incident to this proof.

With the eye in any given position R_a stimulation of an individual extraocular muscle induces a contracting force which is a function of the degree of stimulation and of the length of the muscle. This

* It seems possible that as the limit of the fusional stimulus is reached, attempts at physiologic compensation might in some such instances take the form of rapid alternation which in time might facilitate lower-level feed-back circuits so as to result in a rotary (torsional) nystagmus. This would seem more likely if there were little or no dominance of one eye. We are here entering a field of conjecture, however, which we are not at present ready to explore. We mention rotary nystagmus only because it may be an associated phenomenon of alternating hypertropia, and because in three such cases treated surgically during the past six months the rotary nystagmus almost completely disappeared immediately; in all these cases, the surgery was aimed principally at decreasing the extorsional effects of the inferior obliques.

exerts a torque on the globe acting from its point of contact with the globe toward its origin. The rotational effect of this torque (or moment) is equal to the force F times the *moment arm* from the center of rotation to the line of action of the muscle. This moment arm can be resolved into components acting for horizontal, vertical and torsional rotations, respectively.

The length of the muscle can be expressed as a function of the component angles of rotational position, since its origin remains fixed to the skull and its insertion varies (with respect to the skull) according to the position of the globe. Thus, $l = f(H, V, T)$, and this function is nonlinear in each variable (and it is complex!).* Now the rate of change in length of the muscle with respect to change in each of the three components of rotational position, for any given position of the globe R_a , is given by the three partial derivatives of this function. Therefore, the component moment arms for horizontal, vertical, and torsional rotation are seen to be

$$\frac{\partial f(H, V, T)}{\partial H}, \quad \frac{\partial f(H, V, T)}{\partial V}, \quad \text{and} \quad \frac{\partial f(H, V, T)}{\partial T},$$

respectively, when H_a , V_a , and T_a are appropriately substituted for corresponding variables.

But these partial derivatives are themselves nonlinear functions which differ from each other according to which component is considered variable, and which assume unique values for each and every position of the globe. Therefore, not more than one of the three can change by exactly the same amount over any interval H_a to H_{a+b} as over the interval H_{a+b} to H_{a+2b} , nor over any interval V_a to V_{a+b} as over the interval V_{a+b} to V_{a+2b} , nor over any interval T_a to T_{a+b} as over the interval T_{a+b} to T_{a+2b} . Hence, they must change differently for any change in position from

R_a to R_{a+b} than for a change in position from R_c to R_{c+b} , even if $R_c = R_{a+b}$; and this will hold true even if any two of the changes in positional components represented by b (that is, H_b , V_b , and T_b) are equal to zero.

Furthermore, since the lines of actions of the direct antagonists are not all symmetric with respect to the globe for any position whatever, the obliques normally being appreciably asymmetrical in situations where the vertical and horizontal recti are symmetrical, the summation of the individual changes in each of the component moment arms, for all six extraocular muscles considered together, must still be different for the change in position from R_a to R_{a+b} than for the change in position from R_c to R_{c+b} . Neither can the effects of changes in lengths of the muscles on their contracting forces, nor the effects of changes in extraocular muscle proprioceptive impulses on the "conjugate mechanism," nor the changes in elastic (passive) forces from differing stretches of connective tissue connections to the globe, balance out these differences exactly. All of these functions are of dissimilar forms; and with no (habitual) cause to become modified so as to approach a balancing out in their combined effects, they can only increase or decrease such differences in a non-uniform manner. Therefore, there must be a difference in the change in the final motor stimulation pattern, and also in the change of conjugate stimulation, for moving R_a to R_{a+b} on the one hand, and for moving R_c to R_{c+b} (or for moving L_c to L_{c+b}) on the other hand. This completes the formal proof.

This "proof" is not so much geometric as it is a statement of probabilities. To summarize briefly, if the total moments acting on the two eyes cause them to reach equilibrium at the positions R_a and L_{a+b} , then a change of moments causing R_a to become R_{a+b} is not likely to cause L_{a+b} to become L_{a+2b} . This is because the moment

* Derivation of such functions, and numerical substitutions, will be included in another paper.

arms, muscle lengths, passive forces, and so forth, change in such a complex and highly asymmetrical manner that a unique set of tensions would have to be expected from the extraocular muscles of each eye in order for them to maintain exactly the same relative positions of deviation after such movement. Since there is no stimulus of fusion to mold such a play of tensions, it is outside the realm of probability to expect them to assume exactly the unique values which would be demanded.

C. INTERPRETATIONS

It is important to note the qualification "exactly" in Theorem II. If the initial deviation of the two eyes is small, after a change in conjugate stimulation the deviation is likely to be nearly the same for each component. The differences demanded by Theorem II often will not be measurable, or more frequently will not be sufficiently consistent to measure with any certainty. Inconsistencies result from difficulty in completely eliminating fusional (including accommodative) influences, and from moment to moment variations in the fatigue of neurones or muscle, "creep" of elastomeric tissues connected to the eye, possibly variations in the lower-order tonic impulses to the muscles, and so forth. Inconsistencies which result from various of these factors are constantly apparent in successive measurements of normal "muscle balance," especially if taken at different times, more so if taken after measuring vergence powers, and even more so if taken with differing techniques which exclude fusional influences to differing degrees.

However, if the initial deviation is large, these variations generally will not completely mask the differences in the components of deviation when the positions of the eyes are altered by conjugate stimuli. In certain situations the differences are readily apparent even when the initial deviation is small: this is often the case in double hypertropia. Finally, differences may be obvious on alternate fixation in the

primary direction, as is true in cases of double hypertropia, or they may be readily apparent only when the eyes are directed alternately in some other direction(s).

The conjugate mechanism develops in large part from postural and other primitive reflex arcs which are patterned anatomically to produce qualitatively comitant movements of the two eyes with respect to any one of the three rotational components. Consequently, a change in conjugate stimulation which will cause a purely horizontal, a purely vertical, or a purely torsional rotation of one eye will cause the other (deviated) eye to rotate so that same component is similarly directed, although of more or less different magnitude. Rotation of the second eye will also, however, include each of the other two components. The two components which differ from zero only for the second eye are conveniently designated as "secondary." Each of these secondary rotations may be positive or negative in direction, and each of them may or may not be significant in magnitude, dependent on the particular situation.

Reversing the direction of purely horizontal, purely vertical, or purely torsional rotation of the one eye should always result in reversing the direction of that same component, and usually in reversing the directions of the secondary components of rotation of the deviated eye. The qualification "usually" covers occasional situations where the rotations occur about points of inflexion in the rates of change for one or both of the other two components.

VII. ANALYSIS

A. THE GENERAL CASE

For the general case, we need only consider movement of the eyes between R_aL_o and R_oL_b , because the same arguments would apply for alternate fixation in positions R_aL_i and R_iL_b . From Theorem II, the change in conjugate stimulation required to move R_a to R_o will *not* result in rotations

of the left eye away from its fixating position exactly equivalent to the rotations of the right eye into its fixating position. To see what *will* result, let us imagine the right eye rotates from R_n to R_0 in three separate steps, by components $-H_n$, $-V_n$, $-T_n$, and analyze the simultaneous rotations of the left eye:

$$\text{Step 1 } \begin{cases} R(H_n, V_n, T_n) \rightarrow R(0, V_n, T_n) \\ L(0, 0, 0) \rightarrow L(H_{-h}, V_{(\pm)h}, T_{(\pm)h}) \end{cases}$$

$H_{-h} (= -H_h)$ is of the same sign as $-H_n$,

but $V_{(\pm)h} (= (\pm)V_h)$ and $T_{(\pm)h} (= (\pm)T_h)$ represent secondary rotational components either of which may be plus or may be minus, depending on the particular situation.

$$\text{Step 2 } \begin{cases} R(0, V_n, T_n) \rightarrow R(0, 0, T_n) \\ L(H_{-h}, V_{-h}, T_{(\pm)h}) \\ \rightarrow (H_{-h(\pm)v}, V_{(\pm)h-v}, T_{(\pm)h(\pm)v}) \end{cases}$$

V_{-v} has the same sign as $-V_n$, but $H_{(\pm)v}$ and $T_{(\pm)v}$ may be plus or may be minus.

$$\text{Step 3 } \begin{cases} R(0, 0, T_n) \rightarrow R(0, 0, 0) \equiv R_0 \\ L(H_{-h(\pm)v}, V_{(\pm)h-v}, T_{(\pm)h(\pm)v}) \rightarrow L(H_{-h(\pm)v(\pm)t}, V_{(\pm)h-v(\pm)t}, T_{(\pm)h(\pm)v-t}) \equiv L_h \end{cases}$$

T_{-t} has the same sign as $-T_n$, but $H_{(\pm)t}$ and $V_{(\pm)t}$ may be plus or may be minus.

Now

$$D_{RL} = \begin{pmatrix} \Delta H = H_n \\ \Delta V = V_n \\ \Delta T = T_n \end{pmatrix}$$

and

$$D_{RL} = \begin{pmatrix} \Delta H = -H_b = H_b(\mp)H_v(\mp)H_t \\ \Delta V = -V_b = V_v(\mp)V_h(\mp)V_t \\ \Delta T = -T_b = T_t(\mp)T_h(\mp)T_v \end{pmatrix},$$

where the notation (\pm) or (\mp) is used to emphasize that the quantity may be positive or may be negative, depending on the given situation, but cannot be both for the same situation, and hence does not represent two separate answers.

Finally,

$$D_{RL}^{RL} = \begin{pmatrix} \overline{\Delta H} = \frac{H_h + H_n(\mp)H_v(\mp)H_t}{2} ; \overleftrightarrow{\Delta H} = \pm \frac{H_h - H_n(\mp)H_v(\mp)H_t}{2} \\ \overline{\Delta V} = \frac{V_v + V_n(\mp)V_h(\mp)V_t}{2} ; \overleftrightarrow{\Delta V} = \pm \frac{V_v - V_n(\mp)V_h(\mp)V_t}{2} \\ \overline{\Delta T} = \frac{T_t + T_n(\mp)T_h(\mp)T_v}{2} ; \overleftrightarrow{\Delta T} = \pm \frac{T_t - T_n(\mp)T_h(\mp)T_v}{2} \end{pmatrix}.$$

In alternating hypertropia which is not combined with a simple hypertropia of greater degree (that is where the alternate vertical deviations are actually oppositely directed), ΔV_{RL} must be of different sign than $\overleftrightarrow{\Delta V}_{RL}$ (or stated in another way, $|\overleftrightarrow{\Delta V}| > |\overline{\Delta V}|$). This condition is fulfilled if and only if the algebraic sum of $(\mp)V_h$ and $(\mp)V_t$ is of greater magnitude than, and of opposite sign from, V_v . But V_h and V_t represent changes in vertical deviation

which are "secondary" to horizontal or torsional rotations which must take place during alternate fixation because of horizontal or torsional deviations, respectively. Therefore the oppositely directed vertical deviations of alternating hypertropia must be "secondary" to horizontal and/or torsional deviations.

The existence of a double hypertropia which may or may not be combined with a "simple" hypertropia of greater degree

demands only that

$$\Delta V = \pm \frac{V_v - V_h(\mp)V_h(\mp)V_t}{2} \neq 0.$$

Now V_v approaches V_h in magnitude, and nearly cancels it out in the expression for ΔV ; also, double hyper is seldom readily apparent unless any appreciable ΔV is compensated for (by prisms or amblyoscope) during the examination. Therefore the presence of any detectable ΔV is dependent essentially on the condition $(\pm)V_h(\pm)V_t \neq 0$, and double hyper in general must be secondary to horizontal and/or torsional deviations.

Theoretically, double hypertropia should be found in every squint, for alternate fixation in any other than some one possible direction where $(\pm)V_h(\pm)V_t$ might happen to balance out the difference between V_v and V_h . Practically, this is not true, for reasons given in the discussion of Theorem II. However, at least minute amounts of ΔV can be found in a large proportion of squints where cooperation is excellent and where the examination is sufficiently exhaustive. Furthermore, the frequency of significant amounts of ΔV has already been indicated; and any significant ΔV decreases the proportion of time a patient is able to maintain bifixation, consequently tends to progressively decrease his fusion ability, and thereby gives other (latent) deviations more chance of becoming manifest.

Any measurable ΔV , which represents double hypertropia still apparent while the average horizontal and vertical deviations (ΔH and ΔV) are symmetrically compensated for, must obviously be secondary to torsional deviation alone. Consequently $\Delta V - \Delta V$ may conveniently be considered as representing the amount of double hyper which is secondary to horizontal deviation (but still is influenced by the torsional deviation, *not* the amount secondary to the horizontal deviation alone—see later).

Changes in horizontal and in torsional deviations incident to alternate fixation may be analyzed in an analogous manner. Very briefly:

1. ΔH_{RL} will be of different sign from ΔH_{RL} , indicating an *eso-* with the one eye fixating and an *exo-* with the other, if and only if $|(\pm)H_v(\pm)H_t| > |H_h|$ and also $(\pm)H_v(\pm)H_t$ is of opposite sign from $-H_h$. There will be at least a quantitative difference in ΔH incident to alternate fixation if

$$\Delta H = \pm \frac{P_h(\mp)H_v(\mp)H_t - H_h}{2} \neq 0.$$

The large variation in ΔH itself from fusional stimuli usually obscures any ΔH , and the comparatively large horizontal vergence powers generally render it of little or no importance.

2. A quantitative difference in ΔT on alternate fixation is indicated by

$$\Delta T = \pm \frac{T_t(\mp)T_h(\mp)T_v - T_a}{2} \neq 0.$$

An *excyclo-* with one eye fixating ($+\Delta T$) and an *incyclo-* with the other ($-\Delta T$) will be present if $|\Delta T| > |\overline{\Delta T}|$, which occurs if and only if $|(\mp)T_h(\mp)T_v| > |T_t|$ and also

$$|(\mp)T_h(\mp)T_v + T_t| < |(\mp)T_h(\mp)T_v - T_t|.$$

Correction of the fundamental horizontal and vertical deviations should essentially eliminate any ΔT .

B. DIRECTIONALLY VARIABLE ΔV

Even if there is complete equivalence of the two eyes in the primary direction (with either eye fixating), there still may be deviations for fixation in other directions, to whatever extent the conjugate mechanism is not precise. Theoretically, there may be a variable deviation of this nature, with differing components ΔH , ΔV , and ΔT for each and every direction of fixation R_L and R_L except where $a=0$. Some directionally-variable deviation of

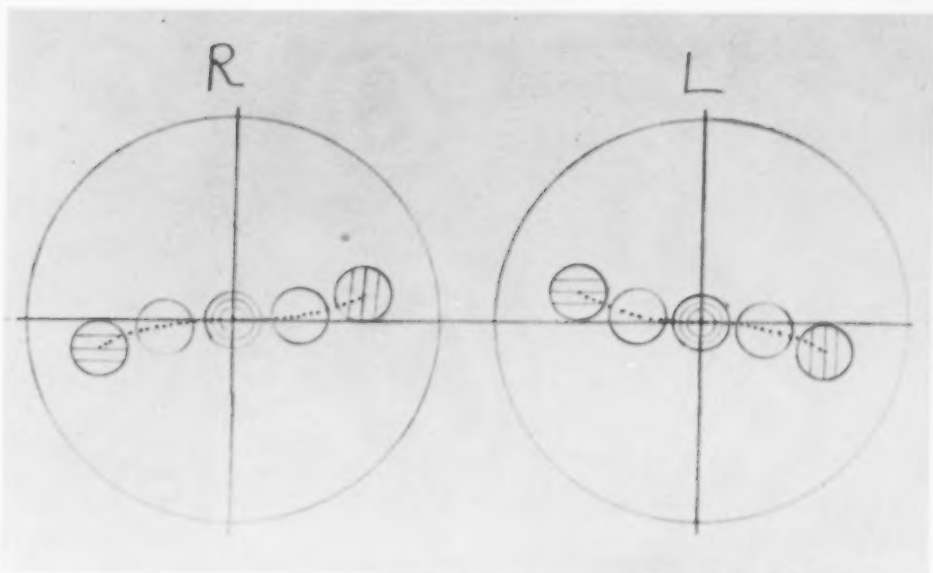


Fig. 10 (Guyton and Kirkman). Variable ΔV for differing horizontal directions of gaze.

this type is common after primary equivalence has been brought about surgically, unless the surgery has been "guesstimated" fortuitously enough to compensate for the complexities of contracture, creep, asymmetries, improper neurogenic habituation, and other variations which influence abnormal development of the conjugate mechanism. Fortunately, if there is primary equivalence, variations of this sort are not too often important for fixation near the primary position, even in cases where primary equivalence has been attained surgically. A variable ΔV according to the horizontal direction of gaze (fig. 10) is the most noteworthy exception, and rarely a difference in ΔH for upward gaze as compared with downward gaze is of importance.

C. DETAILS FOR DOUBLE HYPERTROPIA SECONDARY TO TORSIONAL DEVIATION

This form of double hypertropia, represented by $\Delta \hat{V}$, is the type which has appeared most puzzling, and is the type to which Theorem I as well as Theorem II applies. The mechanism of this "torsional"

type of double hypertropia is more difficult to visualize than is that of the "horizontal" type. The difficulty in visualizing the mechanism lies principally in understanding that fixation per se involves rotating the eye into the properly equivalent torsional position for the given direction of gaze, regardless of the fixation target, and that consequently the double hypertropia cannot be stopped by simply rotating (torsionally) the fixation target in a major amblyoscope: since the eye will still fixate in its habitually proper torsional position, and the image of the rotated target will not be admitted to the sensorium until the eye does fixate, the perceived image will simply appear to be tilted, as it is.

We will analyze a hypothetical case wherein horizontal deviation is completely insignificant, such that $\Delta \hat{H} \rightarrow 0$ and therefore $\Delta \hat{V} = \Delta \hat{V}$. This analysis will largely concern comparisons of approximate rates of change in moment arms for torsional and vertical rotation as the eyes move into differing torsional positions; minor complexities will be ignored:

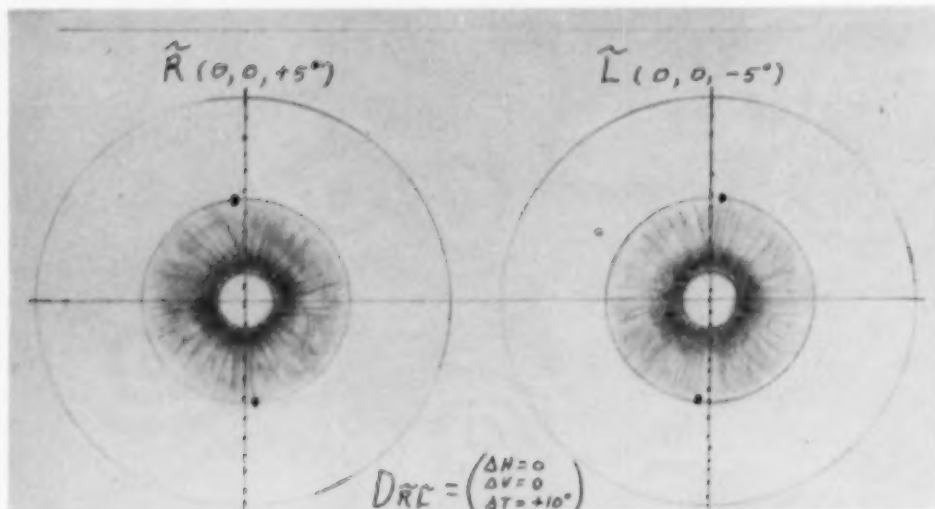


Fig. 11A (Guyton and Kirkman). Positions of physiologic rest for a hypothetical case of symmetrical double hypertropia secondary to torsional deviation.

Let the eyes be in positions of physiologic rest, and let these initial positions be $R(0, 0, +5^\circ)$ and $L(0, 0, -5^\circ)$ (fig. 11A). Supply conjugate stimulation so as to move L to L_0 . If "precise," the change in stimulation reaching R should be such as would move R from $R(0, 0, -5^\circ)$ to R_0 , if its initial position had been $R(0, 0, -5^\circ)$ instead of $R(0, 0, +5^\circ)$.

This imaginary movement of the right eye could be accomplished by increasing the tensions of the inferior oblique (IO) and inferior rectus (IR), and decreasing the tensions of the superior oblique (SO) and superior rectus (SR), by specific amounts such as would not cause any vertical rotation. (We are ignoring the relatively insignificant effects of the horizontal recti, and also ignoring any resulting horizontal movements.)

Now the elevating effect of the IO* is enhanced in a position of extorsion as compared with a position of intorsion, while

the depressing effect of the IR is lessened. Thus an increase in tension of these muscles of such ratio as not to change their combined vertical rotating effect (that is, so the increase in elevating effect of the IO equals the increase in depressing effect of the IR), for a rotation from the intorted position $R(0, 0, -5^\circ)$ to R_0 , if applied in the same ratio with the eye in the initially extorted position $R(0, 0, +5^\circ)$, should result in an *appreciable net elevating effect*. There still would be an extorting effect, but of lesser degree, since the IO becomes less efficient as an extorter in extorsion than in intorsion, while the torsional efficiency of the IR does not change much in this particular situation.

The depressing effect of the SO changes only slightly in positions of relatively small degrees of extorsion, compared with small degrees of intorsion. Whether it is enhanced or diminished depends on the exact positions of its quite variable origin and insertion. The elevating effect of the superior rectus increases in extorsion. Thus a decrease in tension of these muscles, in such ratio as not to change their combined effect for vertical rotations over the im-

* Considering there is partial "locking" of the sheaths of the IO and the IR, as is actually the case: this is taken into account in calculations of moment-ages which will be published in a later paper of this series.

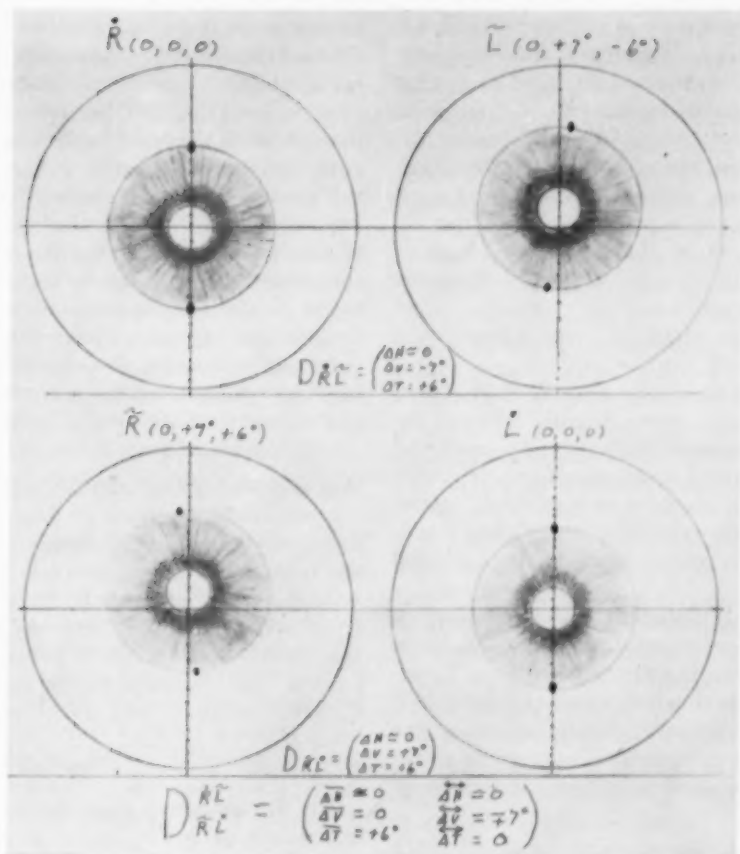


Fig. 11B (Guyton and Kirkman). Same hypothetical case as in Figure 11A. Positions of eyes during alternate primary fixation.

aginary rotation from $R(0, 0, -5^\circ)$ to R_0 , when applied in the same ratio with the eye initially at $R(0, 0, +5^\circ)$, should usually result in some decrease in elevating effect (this decrease being more than offset by the net increase in elevating effect of the two lower muscles in most situations), and some decrease in intorting effect.

Now if the muscle origins and insertions happened to correspond to the average normal, and if the change in stimulation acted equally to decrease tensions in the upper muscles and increase tensions in the lower muscles, the total net effect would be to extort the eye slightly less than five

degrees, and to elevate it a little. But since the position $R(0, 0, +5^\circ)$ is the position of physiologic rest for that eye, the change in stimulation must have the effect of *increasing* the final total muscle tensions [that is, active (neurogenic) + passive (elastic) tensions], so the effects from the lower muscles should predominate, and there should be less net extorting effect and more net elevating effect. The final position, if the muscle origins and insertions were "normally" placed, might well be $R(0, +4^\circ, +8^\circ)$.

But suppose the predominant reason there is any torsional deviation in these imaginary "rest" positions is because the

normal asymmetry of the lines of action of the obliques is exaggerated from anatomic variation in their insertions such that the IO inserts further up the temporal side of the globe and/or the SO inserts further toward the nasal side of the upper aspect of the globe than the normal average;* this could further enhance the net elevating effect obtained from changing the muscle tensions as outlined above, while decreasing the net extorsional effect still further: the final position might well be $R(0, +7^\circ, +6^\circ)$.

Now let us change the conjugate stimulation so as to move R to R_0 . After so doing, if symmetry happens to be exact, the left eye should move from L_0 to $L(0, +7^\circ, -6^\circ)$. (We can think of both eyes as rotating back through their initial positions of physiologic rest during this alternation of fixation.)

Figure 11B depicts the manifestations of this fundamental torsional deviation during alternate primary fixation. To repeat, we have ignored any changes which Theorem II says should occur in the horizontal components, and which might well be too small to measure in this example.

D. DOUBLE HYPERTROPIA SECONDARY TO HORIZONTAL DEVIATION

Double hypertropia secondary to horizontal deviation is designated by $\overset{\leftrightarrow}{\Delta V} - \Delta V$. It is quite common if the horizontal deviation

* Asymmetry of the obliques which might tend to give extorsional deviation could in addition consist of the IO arising more posteriorly or inserting more anteriorly, and/or the SO arising more anteriorly or inserting more posteriorly than the normal average, although these or opposite variations would tend more to cause a directionally-variable average vertical deviation for looking right and looking left. In general, and quite roughly, the more steeply the SO slants posteriorly in comparison with wrapping around the upper equator, the less effectively it can be utilized as an intorter without exerting too much depression, and conversely for the IO. Asymmetry opposite from "normal" may occur rarely and account for double hypo with intorsion. Also, a very shallow posterior slant of the SO combined with insertion far clockwise on the globe, and/or conversely for the IO, could account for double hyper with extorsion.

tion is large, here being a result of the differing horizontal components of rotational position incident to alternate fixation, rather than differing torsional positions alone. If the horizontal component of deviation is predominantly responsible for the phenomenon of double hypertropia (that is, if $\Delta V \rightarrow 0$) the vertical movements of alternately covered eyes can almost or completely be stopped, for any given target-direction, by appropriate horizontal and vertical prisms, and any other lenses necessary to equalize the accommodation-convergence reactions of the two eyes. The mechanism of this type of double hyper is readily visualized if one thinks of their kinship to cases with variable $\overline{\Delta V}$ according to the horizontal direction of gaze, without significant horizontal deviation and without true double hyper, which are customarily diagnosed as "overaction of the inferior obliques" or "bilateral superior rectus paresis" or "bilateral inferior rectus paresis," etc. (Refer to Figure 10.) A more detailed analysis hardly seems necessary.

E. THE BIELSCHOWSKY PHENOMENON

The Bielschowsky phenomenon may be explained as follows:

1. An amblyopic eye attempts to align itself to meridional contours (oblique, vertical, or horizontal) into the equivalent torsional position which is requisite for either eye to fixate the given target, in response to considerably less stimulus than is required for it to attempt horizontal and vertical alignment of its visual axis into the fixating position. The relatively greater reflex for aligning of meridional contours was well proved long ago, although emphasis was directed to vertical or horizontal contours, at the expense of not according oblique contours the equal importance which is their due.

2. As the stimulus to the fixating eye is decreased by the wedge, and the relative stimulus to fixate with the amblyopic eye is consequently increased, that eye reacts by progressively approaching the torsional

position requisite for it to fixate; and as it does so, the component of vertical deviation which is due to its having been torsionally deviated decreases also. Most often the primary torsional deviation will have been extorsion, with vertical elevation the principal secondary rotational component associated with it. If the amblyopic eye finally reaches a level actually below that of the good eye, either (a) the latter has been darkened so it no longer fixates, and itself begins to deviate extorsionally, with associated vertical elevation, or (b) there is also a "simple hyper" element wherein the good eye is higher than the amblyopic one when both are in torsionally equivalent positions for primary fixation.

VIII. SURGERY

A. BASIS

It is not a purpose of this paper to set forth indications for treating double hypertropia surgically, except to say that if surgery is to be utilized, the earlier the better. Neither is it our intention to describe surgical details. Rather, we will indicate a general scheme for planning the surgery. This scheme is based primarily on the foregoing concepts, together with certain approximations learned from reasonable experience. Practically, surgical correction of double hypertropia in the manner outlined here does work out rather well. However, the approximations set forth herewith do not pretend to be anything more than approximations.

B. GENERAL AIMS AND MODES OF PROCEDURE

In general, treatment of alternating hypertropia should be aimed at approaching symmetry as soon as possible after its need becomes apparent, before progressive changes from the altered physiology make symmetry less possible to approach. The term "symmetry" is here utilized in a very broad sense, to include symmetry or equivalence of vision, of accommodation, of positions of the two globes, of their ranges

of motion, and of the "lines of action" of direct antagonists relative to each other and to those of the fellow eye. While some compromise is generally demanded, the desirability of approaching symmetry is constantly kept in mind, especially in choosing between surgical alternatives.

To correct double hypertropia surgically, we should move the positions of physiologic rest into close primary equivalence, except insofar as we should also anticipate "latent" deviational components* which would likely become manifest several days to several months later, and compensate for these (we will designate the total fundamental deviating tendencies as **H**, **V**, **T**) or by boldfaced capitals **H**, **V**, **T**) so as most likely to result in primary equivalence after the eyes have stabilized. This should eliminate the double hypertropia for the primary direction. At the same time, we should apply corrections for any excessive variation in the average vertical deviation for differing horizontal directions of gaze.

We will usually move insertions of obliques for **T**, horizontal recti to correct for **H**, obliques and/or vertical recti to correct for **V**. We will consider all contiguous fibrous attachments integral parts of a muscle insertion, to be moved accordingly. We will measure movement of a muscle insertion in terms of the *effective* change in attachment of its midpoint. Allowances for the gain or loss due to surgical reattachment itself will need be made by the individual surgeon, to correspond with individual surgical techniques.

We will imagine moving muscle insertions about three successively different and

* The positions of physiologic rest reflect the effect of all previous fusional efforts on the state of relative contracture or relaxation of the various muscles and contiguous elastomeric attachments, as well as on "tonic" stimulation of the muscles. Latent deviations in these positions may be likened to the latent portion of a simple hyperphoria which becomes manifest only after the initially evident simple hyperphoria has been corrected by a prism for some time; or to the latent portion of an intermittent exotropia which shows up some time after surgical correction of the initial amount.

mutually perpendicular axes of rotation, the visual, vertical, and transverse global axes, which will serve successively as "polar" axes of rotation. Imagine "circles of latitude" of 0, 30, 45, 60, and 75 degrees for each of these polar axes. The circle of 0-degree latitude in each instance is a great circle, but the other circles of latitude are not. Figure 12 shows such "latitudes," on the temporal aspect of the globe, for vertical rotation about the transverse axis. Here the circle of 0-degree latitude (the term "equator" is avoided because it might be confused with the anatomic equator of the globe) runs around the globe in the plane of the visual and vertical global axes, thus including the macula and the midpoints of the vertical recti insertions. Vertical rotation of the globe with respect to these insertions, or vice versa, should thus consist in moving the insertions along great circle arcs extending from their original midpoints toward the macula or the corneal apex—not along the lines of the vertical recti themselves for the primary position of the globe. On the average, the midpoint of the superior oblique insertion will also be almost on the circle of 0-degree latitude, while that of the inferior oblique will lie at almost 40-degrees latitude (for vertical rotations). However, the positions of these insertions are so variable the approximate "latitudes" they are to be rotated along will need be estimated

during operation. Note the average position of the posterior tip of the inferior oblique insertion is near the 0-degree circle of latitude, which moves the greatest distance during vertical rotation, while that of the anterior tip is near the pole (in this instance the transverse axis), which does not change position during vertical rotation.

For horizontal rotation, around the vertical axis of the globe as a pole, the midpoints of the horizontal recti insertions should move along the 0-degree great circle of latitude which includes the visual and the transverse global axes—hence toward the macula or corneal apex, along directions these muscles follow when the globe is in its primary position.

For torsional rotation around the visual axis, which is now the "polar" axis, the anatomic equator of the globe corresponds fairly closely to the 0-degree circle of latitude, to which the others are parallel. Note the average midpoint of the superior oblique insertion is at about 25-degree latitude, while that of the inferior oblique is at about 40-degree latitude (for torsional rotation).

In planning movement of the muscle insertions, we will plan torsional movement of the oblique insertions first, and plan any vertical movement of these muscles as starting from their initially indicated points of reinsertion, since allowance will be made for the effects of correcting torsional "tilt" of the vertical and horizontal global axes of the two eyes before calculating the vertical rotations needed. Planned and measured in this order, the final positions for reinsertion of the obliques will more closely approach the theoretical.

Since the actual "latitudes" utilized in moving the obliques will vary considerably for different cases, it is well to have an idea of the relationships between rotation of the globe in degrees, and lengths of arc for various "latitudes":

For a globe of 24 mm. diameter, 1.0 mm. of great circle arc = 4.8 degrees rotation, while 1.0 mm. along the 15-degree circle of

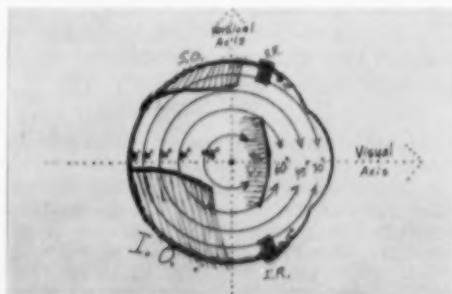


Fig. 12 (Guyton and Kirkman). Diagram of muscle insertions on lateral aspect of right eye, projected on a flat surface. Transverse axis is perpendicular to paper and serves as "polar" axis for vertical rotations: points on surface move along "circles of latitude" indicated in the diagram.

latitude = 5.0 degrees rotation, 1.0 mm. of 30-degree arc = 5.6 degrees, 1.0 mm. of 45-degree arc = 6.8 degrees, 1.0 mm. of 60-degree arc = 9.6 degrees, and 1.0 mm. arc at 75-degree latitude = 18.5 degrees. Stated the other way around, for every one degree of rotation, a point on the surface of the globe moves an arc distance of 0.21 mm. at 0-degree latitude, 0.20 mm. at 15-degree latitude, 0.18 mm. at 30 degrees, 0.15 mm. at 45 degrees, 0.11 mm. at 60 degrees, and 0.05 mm. at 75 degrees.

To correct any $+H$ of more than 12 degrees, any $-H$ of more than 18 degrees, any V of more than six degrees, or any T of more than six degrees, we will distribute the correction between the two eyes unless asymmetry from "contracture" makes it seem better not to.

For any torsional or vertical component of correction of more than three degrees which is to be applied to a single eye, or any horizontal of more than five degrees, we will usually move both insertions of a pair of direct antagonists. If only one is to be moved, we will rate moving the lateral rectus insertion one fourth, the medial rectus insertion one half, as effective as moving both; the superior oblique one fourth, the inferior oblique one half, as effective as moving both; and the superior rectus one third, the inferior rectus one third, as effective as moving both.

C. PLANNING THE SPECIFIC CORRECTIONS IN COMPONENT PARTS

1. Torsion correction

If there is little preference for fixating with one eye or the other, or if there is bifixation much of the time, distribute T (for more than six degrees) equally between the two eyes. Do this even if one eye extorts more than the other on dissociation. (Frequently, the eye which extorts the more will show the lesser vertical deviation.)

If one eye is amblyopic, it still seems preferable at least partially to distribute torsional correction between the two eyes,

performing one third to one half of the total torsional correction on the fixating eye; however, if surgery is for cosmetic reasons only, and it appears otherwise feasible to attain a cosmetic correction by operating on the amblyopic eye alone, all the torsional correction may be applied to the amblyopic eye unless the alternating subcomponent ΔV is very large.

Exceptions to the above occur where appreciable facial asymmetry, or differences in the sizes of the globes, indicate asymmetry of origins and/or insertions of the obliques of one eye compared to those of the other. However, we are not at present certain enough of the analysis of such cases to set down specific criteria for distributing torsional corrections differently than is indicated above.

Now assume the fundamental torsional deviating tendency T is fully twice the objectively measured (or estimated) ΔT if there is bifixation any of the time, and at least one and one half times ΔT if there is not, even if there is marked amblyopia of one eye. If $|\Delta T| + |\Delta V|$ is larger than 2 ΔT in the one case, or 1.5 ΔT in the other, take this empiric sum, instead, as more closely approaching T .

Conceive of forcibly (manually) intorting each eye such as to correct its portion of the estimated T . About one half of the resistance to thus intorting the individual eye lies in the two obliques (along with their fibrocytic frameworks, sheathes, and adjacent fascial attachments). Because of this, imagine that if the oblique attachments were separated from the globe and held in their same positions, the eye then forcibly intorted twice its portion of the angle T , the oblique attachments sealed back in place, and the globe let go of, it would move back just about far enough to give the desired correction for T^* . Of course, as the globe moved back toward its original

* This assumption of a linear relationship between the arc distance over which insertions are moved, and the resulting rotation of the globe, is not correct, but serves as a reasonable approximation except for large movements.

position, the "lines of action" and hence the various moment arms of these two muscles would be altered some: this could be avoided by rotating the globe through its portion of \mathbf{T} and reattaching the obliques after changing their effective tensions, by shortening the one and lengthening the other, sufficiently to hold the globe in its corrected position. However, error introduced by simply reattaching the obliques after rotation through twice the \mathbf{T} value generally is not significant. We will therefore consider twice its portion of \mathbf{T} to be the approximate number of "degrees of longitude" by which the two obliques need be moved around the globe (considering the visual axis as "polar") to attain the desired torsional correction.

2. Horizontal correction

Assume the fundamental horizontal deviating tendency \mathbf{H} is equal to any $+\Delta\mathbf{H}$, or is 1.5 to 2.0 times any $-\Delta\mathbf{H}$, depending on whether the squint is constant or intermittent. Do not take $\Delta\mathbf{V}$ into account in calculating \mathbf{H} (although we will expect the correction for \mathbf{H} to correct for any $(\Delta\mathbf{V} - \Delta\mathbf{V})$).

Imagine moving the globe around its vertical axis, which now serves as the polar axis, by that proportion of the \mathbf{H} degrees of longitude which is to be corrected by moving that eye, with respect to the insertions of the horizontal recti, and thus calculate the amounts they both need be moved. Move the insertions equal amounts for correcting $-\mathbf{H}$, taking care to sever the insertion of Tenon's capsule from the temporal side of the globe in broad fan-shaped fashion when the lateral rectus insertion is being moved posteriorly.

For correcting $+\mathbf{H}$, redistribute the movements such that the medial rectus is recessed three fourths times the calculated $+\mathbf{H}$ and the lateral rectus is shortened one and one half times the $+\mathbf{H}$ for that eye. Take great care not to pick up any fibers from the anterior aspect of the IO insertion along with the lateral rectus tendon: this

is one of the most frequent and unrecognized surgical mistakes we know of. Also take care to reinsert the muscles along the same great circle (of 0-degree latitude with the vertical axis polar) as the original midpoints of the insertions.

3. Vertical correction

a. For primary equivalence only

Assume the fundamental vertical deviating tendency \mathbf{V} is 1.0 to 1.5 times $\Delta\mathbf{V}$, depending on what proportion of the time the eyes may have bifixated during the preceding months.

We wish to distribute vertical correction between the vertical recti and obliques, and between the two eyes, so as to make the relative positions of oblique and vertical rectus insertions most closely approach the average normal relationships of these sets of muscles, while at the same time moving them by amounts which should correct for \mathbf{V} .

Imagine moving the globe, with respect to insertions of the recti and/or obliques, around its transverse axis as a polar axis (refer back to Figure 12.) Calculate the number of "degrees of longitude" each muscle insertion need be moved to correct for \mathbf{V} in the same general manner suggested for correcting \mathbf{T} : Consider the vertical recti as imparting about two thirds of the effect, the obliques some one third of the effect for vertical rotations near the primary positions.* For example, we could move the insertions of both recti alone one and one half times \mathbf{V} , or move both oblique insertions alone three times \mathbf{V} , if either such movement alone would bring about symmetry instead of disturbing it.)

b. Inclusion of corrections for directional variations in $\Delta\mathbf{V}$

Additional surgical corrections may need be included to compensate for the most important of the directionally variable

* In terms of component moment arms for vertical rotation, the effectiveness of the obliques compared to the vertical recti should be in the ratio of about 2:3 for the eye in its primary position. However,

deviations, where an average relative right hyper appears on looking to the left (that is, $\Delta V > \Delta \bar{V}$) and a left hyper on looking to the right (that is, $\Delta V < \Delta \bar{V}$).

It must be remembered, however, that measurements of the changes in $\Delta \bar{V}$ on looking 30 degrees to the left (ΔV) and 30 degrees to the right ($\Delta \bar{V}$), which are made while there is any ΔT , will include certain changes in $\Delta \bar{V}$ which can be expected to disappear after corrections are applied for T . In fact, we should expect the differences ($\Delta V - \Delta \bar{V}$) and ($\Delta V - \Delta \bar{V}$) to each be reduced in magnitude by about $0.6 \Delta \bar{T}$ where T is corrected for. Intorting the eyes surgically has the effect of rotating the planes of the horizontal recti of the two eyes with respect to each other, along with all other attachments; and the relative change in the planes which horizontal rotations of the visual axes are prone to follow should alter the vertical components for $H = \pm 30$ degrees by approximately \mp one third the actual amount of relative intorsion induced by the surgery, or one third T . (Remember the estimation of T allowed for torsional deviation of the "rest positions" being greater than $\Delta \bar{T}$, and for some latent extorsion.)

Only surgery which may be required to correct for changes in $\Delta \bar{V}$ other than those which are likely to disappear when the fundamental torsional deviation is corrected should be added to the surgery already calculated. Any such "independent" changes in $\Delta \bar{V}$ will probably become apparent from comparing ΔV with $(\Delta V - 1/3 T)$ and $(\Delta V + 1/3 T)$, respectively, and we may designate these values as $V_{H=+30^\circ}$ and $V_{H=-30^\circ}$ —except that if there is bifixation part of the time, so $V = 1.5 \Delta \bar{V}$, then $0.5 \Delta \bar{V}$ must also be added to the values for ΔV and $\Delta \bar{V}$.

the moment arms do not necessarily represent the relationships of the actual moments, which include the muscle tensions. Practically, use of a 1:2 ratio appears more nearly correct for the relative effects of moving the insertions (along vertical arcs) at $H = 0^\circ$.

Correction consists of moving the insertion(s) of the obliques and/or the vertical recti of one or both eyes along vertical arcs. To calculate the required movements, remember the relative effectiveness of the obliques compared to the vertical recti (for vertical rotations) is halved at 30 degrees abduction or doubled at 30 degrees adduction. It goes without saying that such changes in muscle attachments will need to be incorporated, with the ones required to move the eyes into equivalent positions for fixation in the primary direction, in a mutually consistent manner.*

D. APPLICATION

a. An illustration

Let us plan the surgical correction for the case depicted in Figures 9A, 9B, 9C, and 8D, with the additional information that the squint is alternating, the eyes are of normal (adult) size, and each eye is emmetropic and has 20/15 vision and normal accommodation. The pertinent measurements for this case are as follows:

$$\Delta H = +30^\circ$$

$$\Delta \bar{V} = -4^\circ$$

* A general solution for distributing the vertical corrections to correct for $V_{(H=+30^\circ)}$ and $V_{(H=-30^\circ)}$, as well as for V is as follows:

Let U_R be the downward rotation of the right eye, around $H=0$, to be brought about by moving its vertical recti; and O_R the downward rotation from moving its obliques. Let U_L and O_L indicate similarly effected rotations of the left eye.

To correct for V , make

$$(1) \quad U_R + O_R - U_L - O_L = V.$$

To correct for $V_{(H=+30^\circ)}$ make

$$(2) \quad \frac{U_R}{2} + 2O_R - 2U_L - \frac{O_L}{2} = V_{(H=+30^\circ)}$$

To correct for $V_{(H=-30^\circ)}$,

$$(3) \quad 2U_R + \frac{O_R}{2} - \frac{U_L}{2} - 2O_L = V_{(H=-30^\circ)}$$

We thus have three simultaneous equations in 4 unknowns, and we may obtain a solution by arbitrarily setting any one of the unknowns equal to zero or to any other value we wish, and solving for the other three: the number of possible solutions is theoretically infinite.

$$\Delta T = +12^\circ$$

$$\Delta V = \mp 12^\circ$$

$$\Delta V = +6^\circ$$

$$\Delta V = -14^\circ$$

Torsional correction

$T = 2 \Delta T$ or $= \Delta T + \Delta V$ (whichever is larger)

$$\therefore T = 24^\circ$$

Distribute one half T ($= 12$ degrees) to each eye. Move each oblique counterclockwise on the right globe by $2[1/2 T]$ or 24 degrees, clockwise on the left globe by 24 degrees.

Movement of the superior oblique will probably be along a "circle of latitude" some 25 to 30 degrees posterior to the equator, and the effective movement should be 4.5 mm. along this arc.

Movement of the inferior oblique insertion will probably be along a "circle of latitude" some 40 to 45 degrees posterior to the equator, and the effective movement should be 3.5 mm. along such an arc.

Horizontal correction

$$H = +\Delta H = +30^\circ$$

Distribute $1/2 H$, or 15 degrees, to each eye. Recess each medial rectus $3/4 \cdot 15^\circ = 11 1/4^\circ = 2.3$ mm. Advance (and/or recess) each lateral rectus $1.5 \cdot 15^\circ = 22 1/2^\circ = 4.6$ mm.

Vertical correction

$$V = \Delta V = -4^\circ$$

$$V_{(H=+30^\circ)} = (\Delta V - 1/3 T) = -2^\circ$$

$$V_{(H=-30^\circ)} = (\Delta V + 1/3 T) = -6^\circ$$

Theoretically, we could correct for V by distributing its correction equally between the obliques and the vertical recti of either or both eyes, without disturbing the relative vertical deviations on looking to the left and looking to the right. The latter could then be corrected for by rotating

each eye downward one and one third degrees with respect to the obliques alone.

Practically, however, we should compromise slightly. We do not want to move a vertical rectus at the same time we move both horizontal recti and both obliques. It is evident from simple inspection that movement of the left eye downward with respect to obliques alone, by an amount which should correct for $V = -4.0$ degrees, should correct for $V_{(H=+30^\circ)} = -2.0$ degrees at the same time, and should only slightly overcorrect for $V_{(H=-30^\circ)} = -6.0$ degrees. Since the measurements themselves, let alone the formulas for $V_{(H=+30^\circ)}$ and $V_{(H=-30^\circ)}$, cannot be expected to be this accurate, we should plan our vertical correction accordingly. This will involve rotating the left eye downward with respect to each oblique insertion by $3 V$, or 12 degrees. Thus the LSO will need be moved posteriorly some 2.0 to 2.5 mm., and the LIO moved anteriorly some 2.0 to 2.5 mm., depending on which "latitudes" (for vertical rotation) the plans for correcting T called for them to be reattached along.

b. For the general case, in brief

We need these measurements: ΔH , ΔT , ΔV , ΔV , ΔV , ΔV .

From whence we calculate:

1. If bifixation is not present any of the time,

$$+H = (+\Delta H)$$

or

$$-H = 1.5 (-\Delta H)$$

$$T = 1.5 \Delta T$$

or

$$|T| = |\Delta T| + |\Delta V|$$

whichever is larger

$$V = \Delta V$$

$$V_{(H=+30^\circ)} = (\Delta V - \frac{1}{3}T)$$

$$V_{(H=-30^\circ)} = (\Delta V + \frac{1}{3}T)$$

2. If bifixation is present part of the time,

$$\begin{aligned}
 +H &= (+\Delta H) \\
 &\text{or} \\
 -H &= 2(-\Delta H) \\
 T &= 2\Delta T \\
 &\text{or} \\
 |T| &= |\Delta T| + |\Delta V| \left\{ \begin{array}{l} \text{whichever is} \\ \text{larger} \end{array} \right. \\
 V &= 1.5 \Delta V
 \end{aligned}$$

$$V_{(H=+30^\circ)} = (\Delta V - 1/3 T + 1/2 \Delta V)$$

$$V_{(H=-30^\circ)} = (\Delta V + 1/3 T + 1/2 \Delta V)$$

And we distribute corrections:

T between both eyes if >6.0 degrees, and to both obliques equally if portion for that eye >3.0 degrees; if the latter is <3.0 degrees, may use only one oblique, rating movement of SO alone one fourth as effective, and IO alone one half as effective, as moving both.

+H between both eyes if >12 degrees, **-H** between both eyes if >18 degrees. The portion of **H** to one eye, between both horizontal recti if $H > 5.0$ degrees. For **+H**, move medial rectus three fourths, lateral rectus 1.5 times the **+H** for that eye. For **-H**, move each of these by the **-H** for that eye. If **H** for an eye <5.0 degrees, and only one insertion is moved, rate movement of LR alone one fourth as effective and MR alone one half as effective as moving both.

V, $V_{(H=+30^\circ)}$, and $V_{(H=-30^\circ)}$ between the vertical recti (U) and the obliques (O) of the two eyes so:

$$\left. \begin{aligned}
 (1) \quad U_R + O_R - U_L - O_L &= V \\
 (2) \quad U_R + 4O_R - 4U_L - O_L &= 2V_{(H=+30^\circ)} \\
 (3) \quad 4U_R + O_R - U_L - 4O_L &= 2V_{(H=-30^\circ)}
 \end{aligned} \right\}$$

where one of the unknowns is arbitrarily set (usually so U_R or $U_L = 0$) and the others determined so as to involve as few muscles as feasible, avoiding work on *any* vertical recti if this can be done with small compromise and without distributing **V** of

more than 6.0 degrees to one set of obliques. Rate movement of both vertical recti two thirds, both obliques one third as effective as moving both sets. For correcting a **V** of no more than three degrees, rate movement of one rectus one third as effective as moving both; or the SO one fourth, the IO one half as effective as moving both.

Should there be any reasonable bifixation reflex, errors in surgical correction are compensated for to a truly amazing extent. Fortunately!

IX. SUMMARY

During alternate fixation and dissociation of the two eyes, properly equivalent spatial orientation demands they fixate in torsionally equivalent positions. In alternating hypertropia those portions of the oppositely directed vertical deviations manifest on alternate fixation, and which cannot be eliminated by prisms or other optical means, are secondary to a fundamental torsional deviation of the two eyes. Surgical correction of the torsional deviation stops alternating vertical deviations of this type.

Any portions of the oppositely directed vertical deviations which can be stopped by compensating for a coincident horizontal deviation may conveniently be regarded as secondary manifestations of the latter. Surgical correction of the fundamental horizontal deviation eliminates alternating vertical deviations of this sort.

Certain alternations or variations in vertical deviations for differing horizontal directions of gaze (*not* true alternating hypertropia) are to be expected in the presence of torsional deviations. However, if such variation is present beyond the degree expected from a given torsional deviation, surgical correction can be planned also to halt the part which is independent of the torsional deviation, and at the same time to correct any fundamental vertical deviation which may coexist.

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OPHTHALMIC MINIATURE

Cure for Squinting

The method of cure, which he proposes as the true one, is, that when the child is arrived at such an age as to be capable of observing directions, he is then to be placed directly before the operator, who directs him to close the undistorted eye, and to look at him with the other. When you find the axis of this eye fixed directly upon you, says the doctor, bid him endeavour to keep it in that situation and to open his other eye. You now see the distorted eye turn away from you towards the nose, and the axis of the other eye will be pointed towards you; but with patience and repeated trials, he will, by degrees, be able to keep his distorted eye fixed upon you, at least for some little time, after the eye is opened; and when you have brought him to keep the axes of both eyes fixed upon you, as you stand directly before him, it will be time to change his posture, and to set him first a little to one side of you and then to the other, and then to practise the same thing; when, in all those situations, he can perfectly and readily turn the axes of both eyes towards you, the cure is effected.

H. Colburn, an experienced oculist,

The Art of Preserving the Sight Unimpaired to an Extreme Old Age,
London, 1816.

KERATITIS SECONDARY TO KERATINIZATION OF THE TARSAJ CONJUNCTIVA*

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Baltimore, Maryland

Keratitis secondary to keratinization of the tarsal conjunctiva is probably not an uncommon lesion; however, I have found no previous reports of this condition. It is the purpose of this presentation to discuss the causes of keratinization of the conjunctiva, to describe eight cases in which varying degrees of superficial keratitis resulted from keratinization of the tarsal conjunctiva, and to discuss the treatment of this anomaly.

Normally keratinization of the stratified squamous epithelium of the skin of the lid comes to a rather abrupt conclusion at the mucocutaneous junction which lies at a level just posterior to the openings of the meibomian glands (figs. 1 and 2). From this point to about a millimeter on the under surface of the lid the epithelium retains a stratified squamous arrangement. It then becomes stratified columnar (fig. 3). The cell layers gradually become reduced to two in number and mucous cells appear (fig. 4).

The exact reason for the abrupt cessation of cornification of the superficial cells of the lid margin is not clearly understood. The constant moistening of the cells by tears and protection from drying by mucous plays some part in the abrupt change, but this is not the whole answer. There are instances, such as in keratitis sicca, where the conjunctiva is relatively dry and still the junction remains in its normal position. In other instances that will be mentioned shortly, tearing may be normal or excessive and mucous secretion plentiful, but keratinization of the conjunctiva still occurs.

Lesions which produce cornification of the conjunctival epithelium may be divided into several groups: (1) Drying of exposure of the conjunctival (for example, ectropion or



Fig. 1 (Maumenee). Upper lid.
($\times 9.5$ magnification.)

staphyloma of the globe). (2) Chronic irritation (for example, chronic allergic reaction to drugs or irritation from drugs, such as furmethide or floropryl [di-isopropylfluorophosphate; DFP]). (3) Changes in the epithelial or subepithelial bed; (that is, hyperplasia or tumors of epithelium, subepithelial scarring from trachoma, pemphigus, chemical burns, cauterization, or irradiation). (4) Vitamin-A deficiency.

The exact chemical change within the cells which causes a transformation of mucous to keratinized squamous epithelium is not known.¹ It is recognized, however, that mucocutaneous junctions are not always static ones. Elsewhere in the body, such as in the cervix of the uterus, vagina, nasal mucous membrane, and so forth, the junction can be

* From The Wilmer Ophthalmological Institute of The Johns Hopkins Hospital and University.

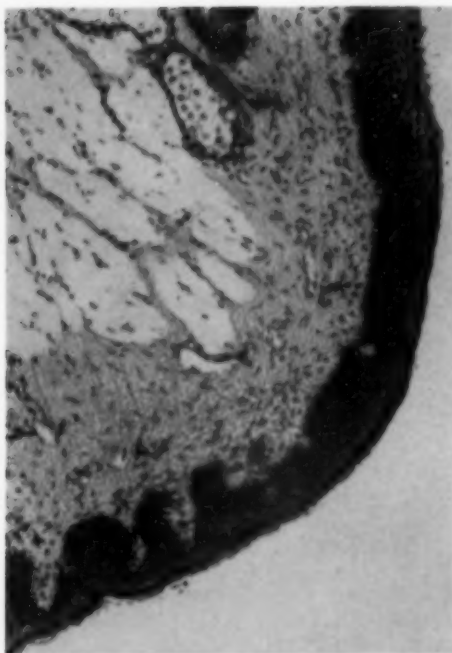


Fig. 2 (Maumenee). Block 1 in Figure 1. Transition from keratinized to nonkeratinized epithelium ($\times 120$.)

shifted by the administration or elimination of estrogen.² Chronic irritation will also produce a similar migration or metaplasia. The subepithelial bed is important in determining the nature of the overlying cells; thus, if all the corneal epithelium is removed, conjunctival epithelium will migrate and cover the normal avascular cornea in a few days. These cells then arrange themselves into stratified squamous epithelium that is typical for the cornea. If the superficial corneal stroma is vascularized in one area, the conjunctival epithelium which covers this area will retain a stratified columnar arrangement with mucous cells.⁸ Similarly scarring in the subconjunctival tissue on occasions produces a conversion to cornified epithelium.

The metaplasia which occurs in vitamin-A deficiency has been extensively studied. Pathologically there is first an atrophy of the mucous cells and epithelium and then a reparative proliferation of the basal cells

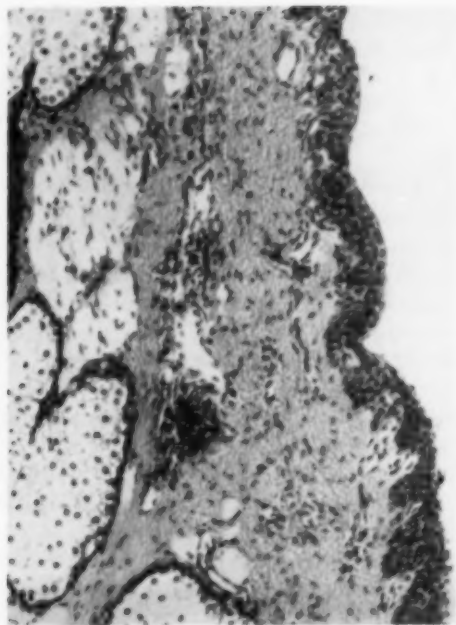


Fig. 3 (Maumenee). Block 2 in Figure 1. Stratified columnar epithelium. ($\times 120$.)

and growth and differentiation of the new cells into stratified keratinized epithelium.³ The administration of vitamin A in the presence of such changes converts the keratinized epithelium to normal mucous secreting tissue again.

Impressive evidence that vitamin A acts directly upon the component tissue is furnished by the experiments of Fell and Melanby.⁴ Explants obtained from the trunk and limbs of six- to seven-day-old chick embryos were placed in tissue cultures containing 1,000 to 3,000 international units of vitamin A per 100 milliliters of tissue culture fluid. The normal amount of vitamin A in the plasma of fowl varies from 200 to 350 international units per 100 milliliters. Within seven days after the skin was placed in the tissue fluid containing excessive amounts of vitamin A, the normal keratinized epithelium had been converted into mucous epithelium with mucous cells. In many instances ciliated cells very similar to those in the nose appeared. When these cultures were

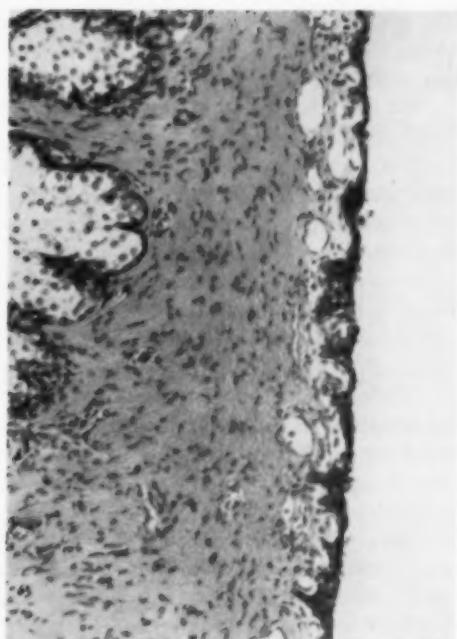


Fig. 4 (Maumenee). Block 3 in Figure 1. ($\times 120$.)

transplanted back to media without the addition of vitamin A, the tissues were converted back to keratinized epithelium in four to five days.

In the conditions listed above where the mucous membrane of the conjunctiva is converted into keratinized epithelium, as in drying, vitamin-A deficiency, or occasionally after drug irritation, the metaplasia is reversible and disappears after the basic cause is corrected; however, in other instances, such as after drug irritation or changes in the subepithelial tissue, the keratinized areas are more lasting, especially if they are connected with the skin epithelium. In many instances of the latter type the lesion will persist even after the irritative agent is discontinued or the active disease process arrested. In some cases the lesion will recur even after it has been removed surgically. It is of interest that cornification begins on the bulbar conjunctiva in vitamin-A deficiency and on the palpebral conjunctiva after chronic drug irritation.

In most of the conditions which have just been described the basic cause of the cornification has been associated with chronic irritation or at least an inflammatory cell reaction in the subepithelial tissue, so that it is not possible to say that the keratin formation produced irritation of the eye. There are other conditions, however, in which it is known that keratinized epithelium produces an irritation of the conjunctiva and cornea. Examples of this type are:

1. Transplantation of skin to the eye to prevent the recurrence of a pterygium.
2. Transplantation of skin to the socket to repair the orbit where mucous membrane is still present in the socket.
3. Surgical procedures where skin is transplanted to the under surface of the upper lid to correct entropion.
4. Warts of the lid margin which come in contact with the corneal surface.

In all of these conditions removal of the keratinized epithelium promptly relieves the irritation of the eye.

CASE REPORTS

Eight patients are to be described in which it was believed that keratitis of varying degrees from a superficial punctate keratitis to ulceration and vascularization of the stroma resulted from keratinization of the tarsal conjunctiva.

CASE 1

P. McK., a white woman aged 30 years. In September, 1952, the patient developed Stevens-Johnson's disease (erythema multiforme exudativum). Following her acute illness she had a reduction in tear secretion and a chronic superficial punctate keratitis. The irritation of her eyes was not improved by the topical or systemic use of cortisone nor by the instillation of methyl cellulose into the cul-de-sac every hour. Her symptoms were relieved if both eyes were closed with pressure bandages.

The patient was first seen by me in consultation on March 5, 1953, at which time

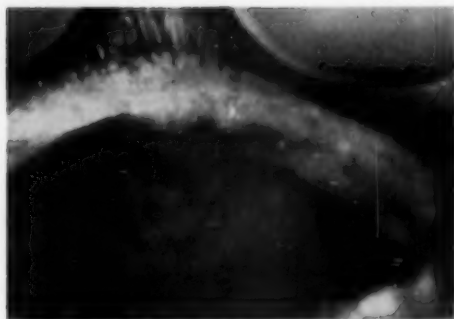


Fig. 5 (Maumenee), Case 1. Migration of keratinized epithelium over the margin of the upper left lid.

she was extremely photophobic. Examination revealed keratinized epithelium on the mucous membrane surface of both upper lids for areas of three to four mm. (fig. 5). The corneas had a ground-glass appearance and on examination with the slitlamp and biomicroscope the epithelium was found to be roughened and edematous. Tears were seen in the lower cul-de-sac, but they did not overflow the lid margin in spite of the extreme photophobia during examination. There was extensive staining of the conjunctiva with one-percent rose bengal solution. Visual acuity was reduced to 20/200 in each eye.

The diagnosis was mild keratitis sicca secondary to Stevens-Johnson's disease and superficial punctate keratitis secondary to keratinization of the tarsal conjunctiva of the upper lids.

The patient returned to her referring physician. The keratinized epithelium was removed from the under surface of the upper lids and a mucous membrane graft from the mouth was inserted into the lid margin. Following this there was no recurrence of the keratinization of the tarsal conjunctiva but the patient's symptoms were only partially relieved.

A sterile solution of the patient's serum was prepared and she used this material to drop into her eyes about four or five times a day. This relieved her photophobia and

her keratitis cleared. Her visual acuity improved to 20/30 in both eyes and has remained at this level for two and a half years.

CASE 2.

J. A., a white boy, age 14 years. The child's eyes were entirely normal until approximately the age of 11 years, at which time he developed Stevens-Johnson's disease.

There was a marked involvement of the right eye with complete obliteration of the cul-de-sacs and a migration of conjunctiva (both epithelial and subepithelial tissue) over the corneal surface. The left eye fared somewhat better with retention of 20/50 vision, but it remained constantly irritated and there was a superficial keratitis with vascularization of the upper half of the cornea.

This eye was treated with topical cortisone, antibiotics, methyl cellulose, and so forth, without favorable response. From April 28 to June 2, 1955, 11-gm. seconds of beta irradiation were given to the upper half of the cornea in an attempt to obliterate the vascularization in this area.

The patient was first seen in consultation on July 27, 1955, at which time it appeared that the right eye was hopelessly lost. There was a complete obliteration of the upper and lower cul-de-sacs with a conjunctival overgrowth of the cornea. Visual acuity was limited to light perception with good projection. In the left eye keratinized epithelium from the skin surface extended over the lid margin onto the posterior surface of the lid for an area of about three mm. This was located in the central portion of the lid and extended horizontally about five mm. There was some obliteration of the upper cul-de-sac and scarring of the conjunctiva in this area. The lashes were in good position and the lids covered the cornea with ease. The upper half of the cornea showed a superficial punctate keratitis with an interstitial vascularization in both the superficial and deep cornea in the corresponding area. The lower half of the cornea was clear. Visual acuity was 20/50. Tearing was normal.

The diagnosis was obliteration of the cul-de-sac with conjunctival overgrowth of the cornea in the right eye, keratitis secondary to keratinization of the upper tarsal conjunctiva in the left eye. The keratinized epithelium was removed from the posterior surface of the left upper lid and a two-mm. wide mucous membrane graft from the mouth was inserted into the lid margin along the entire length of the lid on July 28, 1955. Following this procedure the patient's photophobia and keratitis have cleared.

CASE 3

L. M.,* a Negro aged 42 years. The patient developed keratitis secondary to Stevens-Johnson's disease in July, 1954. He was first seen by Dr. John Gallaher on January 26, 1955, at which time the visual acuity was right eye 20/60, left eye 20/80. There was a marked keratitis sicca with staining of both corneas with fluorescein and rose bengal. The Schirmer test produced only a slight moistening of the filter paper. Cornification of the lid margin was present on the under surface of all four lids (fig. 6). There was an active corneal ulcer in the left eye. Topical antibiotics and methyl cellulose failed to relieve his symptoms.

On May 1, 1955, a mucous membrane graft from the mouth was transplanted to the lid margins of both upper and lower lids on the left side and the keratinized epithelium was removed from the conjunctiva. The corneal ulcer healed, but the visual acuity was not improved due to corneal scarring.

The right eye was treated by wearing airtight goggles which provided a moist chamber. The eye was more comfortable after this, but the keratitis did not clear completely.

On September 23, 1955, the cornified epithelium of the lower lid was removed and a mucous membrane graft inserted into the lid margin. By December 1, 1955, the kera-



Fig. 6 (Mauensee). Case 3. Keratinization of the left upper tarsal conjunctiva.

tinized epithelium on the upper lid had receded to about 0.5 mm. in width.

CASE 4

M. M., a Mexican woman, aged 20 years. At the age of two years, the patient had some type of eczema which caused a marked scarring of her face. The right eye became ulcerated and was removed. An exact history was difficult to obtain on this patient due to language barrier, but apparently the patient had had intermittent attacks of irritation of her left eye.

She was seen at the Stanford University Eye Clinic first in 1949, at which time she was 14 years of age. She had a chronic superficial keratitis with vascularization of the cornea above. Examination of the under surface of the upper lid revealed two small strands of keratinized epithelium about one to two mm. wide, which extended for three to four mm. vertically on the under surface of the lid. The remainder of the conjunctiva appeared smooth and healthy; tearing was normal. The patient was given cortisone and methyl-cellulose drops with no apparent improvement in her condition.

On four occasions the keratinized epithelium was removed from the under surface of the upper lid by curettement and application of silver nitrate. After each removal of the keratinized epithelium there was a transitory relief in the superficial punctate keratitis, but following each treatment the kera-

* This patient is reported through the courtesy of Dr. John A. Gallaher of Walnut Creek, California.

tinized epithelium recurred after a period of several weeks to a month.

By June, 1954 the patient's visual acuity was reduced to 20/200. There was a marked superficial vascularization of the entire corneal surface, and the patient had developed a slight trichiasis. A mucous membrane graft from the mouth was inserted into an incision made in the gray line of the upper lid. The posterior surface of the lid margin and keratinized epithelium on the posterior surface of the lid were removed.

Following this procedure the keratitis cleared and the blood vessels in the corneal stroma decreased in size. By September, 1955, the patient's visual acuity improved to 20/40. There has been no recurrence of the trichiasis nor keratinization of the upper tarsal conjunctiva.

CASE 5

G. F., a white man, aged 38 years. In May, 1953, the patient received a total of 4,192 r to the upper right lid for a basal-cell carcinoma. Following this the tumor was destroyed but there was a complete loss of lashes of the upper lid. His eye was constantly irritated.

Examination on October 22, 1953, showed the left eye to be entirely normal. There was a complete loss of lashes of both the upper and lower lid on the right side. The keratin-

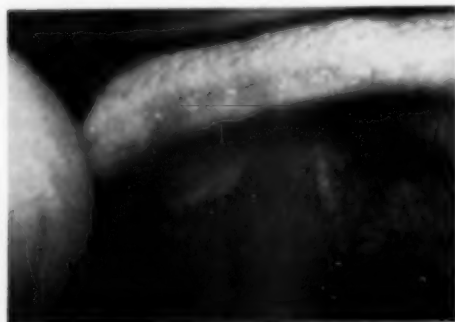


Fig. 7 (Mauumenee). Case 5. October, 1953. Loss of lashes and keratinization of upper tarsal conjunctiva secondary to irradiation for basal-cell carcinoma.

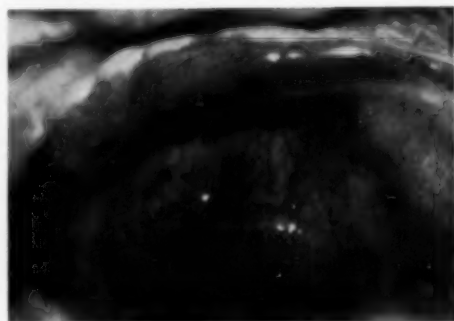


Fig. 8 (Mauumenee). Same lid as Figure 7. December 12, 1954, after mucous-membrane graft to lid margin about four months previously.

ized epithelium of the skin extended on to the tarsal conjunctiva in the central portion of the lid for about four to five mm. in the horizontal and two to three mm. in the vertical plane (fig. 7). The right eye was photophobic and there was a superficial punctate keratitis. Tearing was excessive.

The patient was given a sterile ampule of his own serum which he used as eyedrops. This did not relieve his superficial punctate keratitis.

On April 30, 1954, the epithelium was removed from the under surface of the upper lid. This gave him temporary relief for a period of about two to three weeks, then his chronic irritation returned.

On August 17, 1954, the upper lid was split along the gray line. The posterior margin of the lid was removed and the keratinized epithelium from the under surface of the conjunctiva was dissected away. A mucous membrane graft from his mouth was inserted into the lid margin (fig. 8). Following this the patient was asymptomatic and his punctate keratitis was improved. He was last seen in April, 1955.

CASE 6

L. McC., a white woman, aged 69 years. The patient was seen first in May, 1950, at which time she had bilateral open-angle glaucoma. She was allergic to penicillin, pontocaine, pilocarpine, and many other drugs.

Visual acuity was: right eye 20/400, left eye 2/200. Her course was somewhat stormy, but her glaucoma was finally controlled by multiple operations and miotics.

In April, 1951, she developed keratinization of the tarsal conjunctiva of the upper and lower lids of her left eye. By July, 1951, there was keratinization of the lids of both eyes with chronic punctate staining of the corneas. By November, 1951, she had developed a trichiasis of her left upper lid. The patient was not seen again until November, 1952, at which time she had bilateral entropion of both upper lids with a superficial punctate keratitis on the right and corneal ulceration on the left side. Tearing was excessive.

In December, 1952, a full-thickness mucous membrane graft from the mouth was inserted into the lid margin of both upper lids, and the keratinized epithelium on the under surface of the lids was removed. This corrected the patient's entropion. The corneal ulcer on the left side healed and the superficial punctate keratitis on the right side cleared. Following this the patient had no further trichiasis or entropion and the keratinized epithelium did not return on the tarsal conjunctiva. When she was seen last in January, 1955, the visual acuity in the right eye was 20/50 and her cornea was clear. In the left eye the visual acuity was limited to light perception due to her glaucoma and corneal scarring.

CASE 7

T. R., a white woman, aged 55 years. The patient was seen at the Stanford University Hospital first in January, 1953, at which time she gave a history of having had a conjunctivitis in February, 1952. She was placed on antibiotics and became sensitive to sulfadiazine and penicillin.

In September, 1952, she developed a recurrence of her conjunctivitis which was thought to be on an allergic basis. She was given numerous medications and became sensitive to many of these. In February,

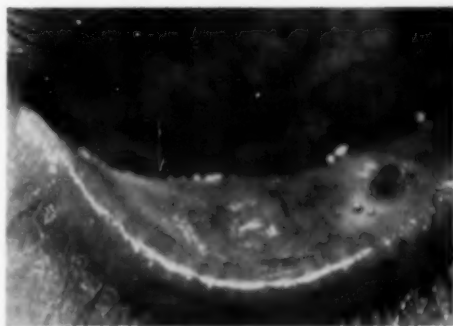


Fig. 9 (Maumenee). Case 7. January, 1953. Marked keratinization of the right lower tarsal conjunctiva.

1953, she developed a corneal ulcer in her left eye.

When she was seen first at the Stanford University Hospital, her visual acuity was 20/80 in the right eye and hand motions at six inches in the left eye. Tearing was reduced in both eyes. There was marked keratinization of the tarsal conjunctiva of all four lids (fig. 9). There was a superficial punctate keratitis and some superficial vascularization of the right cornea. In the left eye there was a dense scar in the stroma secondary to the old corneal ulcer.

The keratinized epithelium was removed from the under surface of the upper and lower lids, first on the left side and then on the right. Following this there was a temporary relief from the keratitis but there was a slight recurrence of the keratinized epithelium on both upper lids, and an entropion developed in both upper lids.

In June, 1955, a mucous membrane graft was inserted into the right upper lid, and in July a similar procedure was done on the left side. She then developed an entropion of the lower lid, and in February, 1955, mucous membrane grafts were inserted into the lid margins of both lower lids. Following this the keratitis was improved somewhat, but was not completely relieved. She was not seen again at the Stanford University Clinic so that the exact cause of the continued irritation of her eyes could not be determined.

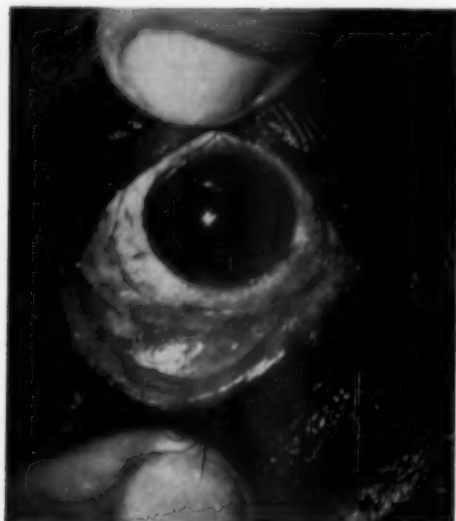


Fig. 10 (Maumenee). *Case 8*. Right eye. Note scarring of cornea below corresponding area of keratinized conjunctiva.



Fig. 11 (Maumenee). *Case 8*. Left eye. Note marked scarring and vascularization of nasal cornea adjacent to cornified tarsal conjunctiva of lower lid.

CASE 8

W. B., a Negro, aged 47 years. The patient was noted first to have chronic open angle glaucoma in the clinic of the Wilmer Ophthalmological Institute in 1948. His intraocular pressure was not controlled on pilocarpine, so in September, 1948, he was placed on furmethide (10 percent four times a day). In August, 1950, he was noted to have a "membrane on the lower tarsal conjunctiva of both lower lids."

On October 25, 1950, the furmethide was discontinued and pilocarpine and eserine instituted. The patient's eyes remained inflamed and he became sensitive to eserine.

The nature of the tarsal conjunctival lesion was not recognized until September, 1955, at which time it was noted that he had corneal scarring and vascularization corresponding to the area of metaplasia of the tarsal conjunctiva in the right eye (fig. 10). In the left eye there was a dense area of scarring on the nasal side of the cornea adjacent to the cornification of the conjunctiva and superficial vascularization around the entire periphery of the cornea

(fig. 11). The patient complained of only mild irritation of his eyes, but there was a superficial punctate staining of both corneas in the areas of keratitis.

In November, 1955, the cornified epithelium was removed from both lower lids and the denuded areas covered with mucous membrane grafts. In the right side mucous membrane from the mouth was used (fig. 12), and in the left the conjunctiva in the upper cul-de-sac was used (fig. 13)



Fig. 12 (Maumenee). *Case 8*. Right eye, 15th postoperative day.

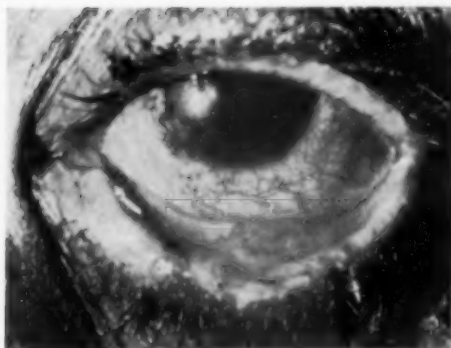


Fig. 13 (Mauernsee). Case 8. Left eye, ninth postoperative day.

DISCUSSION

In 13 eyes of the eight patients just described there was a superficial keratitis secondary to keratinization of the tarsal conjunctiva. In three of these the conjunctival lesion followed attacks of Stevens-Johnson's disease. In two the metaplasia resulted from chronic allergic reaction to topical medication, and one each resulted from irradiation, eczema in early childhood of unknown etiology, and chronic instillation of furmethide for open-angle glaucoma. The clinical appearance of the keratinized epithelium varied from translucent areas to dense white plaques. The former were difficult to find in some cases without the aid of the slitlamp and biomicroscope. One of the most characteristic features was a parchmentlike appearance of the lesion when the lid was everted and allowed to dry for a few minutes. The surface of the lesion was roughened and in most instances was found to be in contact with the skin surface at one point. Occasionally it appeared that the skin of the lid had migrated past the mucocutaneous junction onto the tarsal surface. In a few cases there was no apparent connection between the keratinized areas and the lid margin.

The clinical appearance of the cornification of the conjunctiva is so characteristic that few lesions need to be differentiated from it. Pseudomembranous and membranous con-

junctivitis can be differentiated easily by the moist smooth appearance of the latter as compared to the dry rough parchmentlike surface of the former. The lesions in membranous conjunctivitis are usually much thicker and protrude from the surface of the conjunctiva more than do those areas of keratinized epithelium.

The exact cause of the keratitis associated with cornification of the tarsal conjunctiva cannot be stated; however, it would appear that the most logical explanation is that the rough surface of the hard keratin-containing cells produces a mechanical abrasion of the corneal epithelium. This results in a mild punctate keratitis with edema of the surrounding corneal epithelium. After a period of many months or years the superficial blood vessels invade the edematous corneal stroma. In some instances small areas of ulceration occur with deep vascularization of the stroma. The severity of the keratitis and intensity of corneal scarring appear to be proportional to the duration of the lid involvement. Cases 3 and 8 are particularly suggestive that the cause of the keratitis was a mechanical abrasion due to the roughened epithelium. In Case 3 the area of keratinization was localized in the upper lid only, and only the upper half of the cornea was vascularized. In Case 8 the lower lids of both eyes were cornified and the corresponding area of the cornea showed rather dense superficial scarring and vascularization.

In most of the patients discussed in this series more marked symptoms were produced by involvement of the upper lid than the lower lid. This can be explained by the constant rubbing of the upper lid over the corneal surface.

The areas of cornification of the conjunctiva were associated not only with an irritation of the corneal surface but also with an inflammation in the underlying stroma and tarsus of the lid. Histologic examination shows a chronic inflammatory reaction in the stromal underlying keratinized stratified squamous epithelium (figs. 14 and 15). Like-

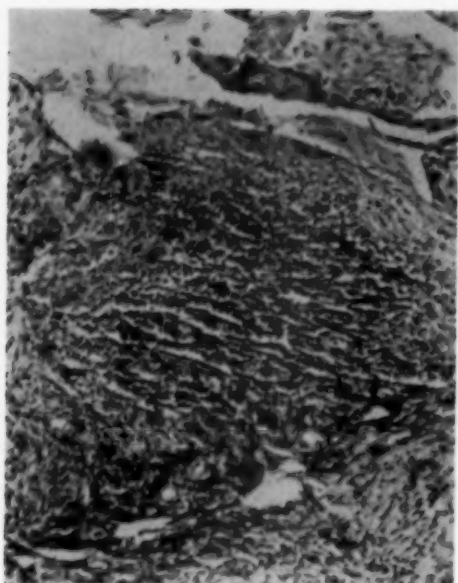


Fig. 14 (Maumenee). Chronic inflammatory reaction in subepithelial area under epithelium from lids in Case 7.

wise, it was noted in one patient (Case 6) that spontaneous entropion occurred after the cornification had been present on the under surface of the lids for a period of approximately one year. In one other patient (Case 7) entropion of all four lids occurred following removal of the keratinized epithelium, and in the third patient (Case 4) trichiasis followed after four removals of the keratinized material.

Medical treatment in the eight cases reported in this series was very disappointing. The only eyes that may have responded to medical therapy were in Cases 1 and 3. These patients were followed by other physicians, and it is somewhat difficult to tell whether their final symptoms were due to a mild keratitis sicca or whether they were the same as those related to keratinized tarsal conjunctiva. In the remaining six patients prolonged use of topical antibiotics, cortisone, methyl cellulose, ointment, or drops of Vitamin A in concentrations up to 50,000 international units per cc., and drops made

out of the patient's own serum had no effect on either the keratitis or regression of the keratinized epithelium. It is obvious that if a patient is known to be allergic to a certain medication or is using any topical medication when he develops keratinization of the conjunctiva, this medication should be discontinued. In this series withdrawal of such treatment did not cause regression of the cornification of the epithelium; however, Cogan⁶ and Leopold⁷ both have observed patients in whom the mucous membrane reverted back to normal after discontinuing a drug which produced irritation of the conjunctiva.

The most satisfactory treatment found in this series of patients was to remove the keratinized epithelium surgically. If the areas were small and not connected with the lid margin, no further treatment was indicated. However, if the lesions were large, removal left a considerable portion of the tarsal area uncovered by epithelium. The reaction which followed led to contracture of the subconjunctival tissue and tarsus and proceeded to entropion. If the keratinized epithelium on the under surface of the lid was in contact with the skin, it usually recurred following its removal.

The following surgical procedure is suggested when the cornified epithelium is in contact with the skin or when trichiasis or

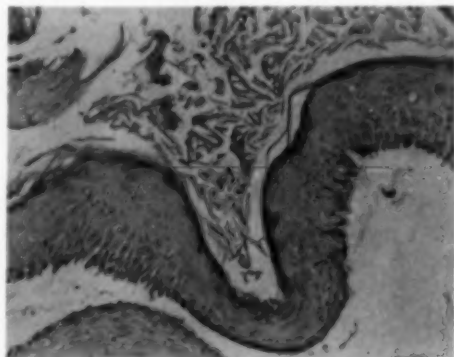


Fig. 15 (Maumenee). Cornification of stratified squamous epithelium same lid as Figure 16.

entropion are associated with the conjunctival lesion, or the area of metaplasia on the tarsal surface is large (one fourth to one half the area). The keratinized area is removed by sharp dissection of the epithelial surface. The lid margin is split at the gray line for almost the full extent of the lid. The tarsus is separated from the orbicularis muscle and skin to make a trough about three mm. deep (fig. 1). The posterior edge of the lid margin which may be covered by cornified epithelium is removed to about square 2 in Figure 1. A thick mucous membrane graft, two to three-mm. wide, is taken from the mouth. The graft is placed in the prepared slot in the lid margin and sutured to the skin surface with 6-0 black sutures and to the tarsal surface with 5-0 plain catgut sutures. Two or three mattress sutures of 5-0 black silk are inserted in the middle of the graft, brought out through the skin three to four mm. above the lid margin (fig. 16). This latter suture aids in tucking the graft into the prepared slot in the lid.

Mucous membrane grafts of this type serve two purposes: (1) They create a new mucocutaneous junction; and (2) they correct any trichiasis or entropion that might have developed. If the entropion is marked, the graft should be correspondingly thicker.

SUMMARY

1. The causes of metaplasia of the mucous

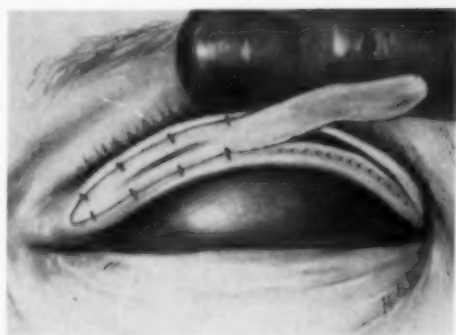


Fig. 16 (Mauensee). Diagram of mucous membrane of mouth being inserted into prepared slot in lid margin.

epithelium of the conjunctiva into cornified epithelium are discussed.

2. Thirteen eyes in eight patients are described in which keratitis resulted from keratinization of the tarsal conjunctiva. The keratitis is thought to be due to mechanical abrasion of the corneal epithelium by the keratin-containing cells.

3. Medical treatment of keratinization of the tarsal conjunctiva was usually unsuccessful in the cases reported and surgical removal of the lesion had to be used.

4. A surgical technique is described for creating a new mucocutaneous junction of the lid margin and for correcting entropion.

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ULTRASONICS IN OCULAR DIAGNOSIS*

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Ultrasonic waves are sound waves which have a frequency above the hearing range of the human ear. This includes all vibrational waves above approximately 20,000 cycles per second. Ultrasonic waves of higher frequency have many features in their propagation characteristic of light waves. They tend to travel in a straight line and may be focused by using a concave crystal. When an ultrasonic beam passes into a medium with characteristics different from the one in which it came, some of it is refracted and some reflected. The amount depends on the difference in the density and elasticity of the two mediums, and the angle at which the beam strikes the new surface.

George Ludwig and Francis Struthers,¹ working at the Naval Medical Research Institute at Bethesda, Maryland, explored the possibilities of detecting gallstones with an ultrasonic "Reflectoscope" and felt that it was feasible. They also demonstrated that large signals would be returned from almost any metal, wood, glass, or plastic foreign body embedded in soft tissues. Wild and Reid² at the University of Minnesota have reported that malignant breast tumors show the largest "echoes" on the Reflectoscope, normal tissue next and benign tumors the smallest reflections.

We felt that the Reflectoscope might be of value in helping to differentiate a simple retinal detachment from one that is the result of a tumor. Because of the difference in the specific acoustic impedance of soft tissues and of various foreign bodies which might

be found in an eye, the Reflectoscope might also aid in diagnosing and possibly localizing intraocular foreign bodies, particularly those which are not opaque to X-rays.

MATERIALS AND METHODS

The basic theory of ultrasonic pulse testing is shown in Figures 1 and 2. A pulse generator sends out a short repetitive high frequency electrical impulse to the transducer or searching unit. This contains a 10-megacycle quartz crystal which converts the electrical impulses into mechanical waves. These ultrasonic waves are then reflected back from the various surfaces and act upon the quartz crystal in a reverse manner to form electrical impulses. These electrical impulses are converted to vertical indications on the screen of the cathode ray tube. Because the speed of the ultrasonic waves is known, the time required for a wave to be reflected from an object can be converted visually on the

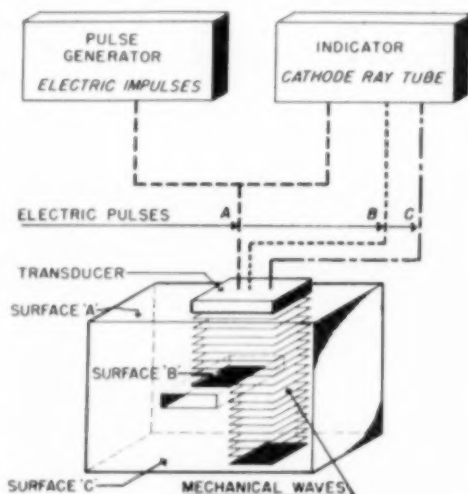


Fig. 1 (Mundt and Hughes). Basic concept of ultrasonic Reflectoscope (taken from manual, *Ultrasonic Testing*, published by Sperry Products, Inc.).

* From the Department of Ophthalmology, University of Illinois College of Medicine. This work was made possible through the kindness of Sperry Products, Inc., who have permitted us to use for three years their ultrasonic "Reflectoscope," and whose representatives, Mr. F. Edward Pringle, Mr. George Slade, Mr. Sheldon Leonard, and Mr. Thomas Cosgrove have given valuable technical advice.

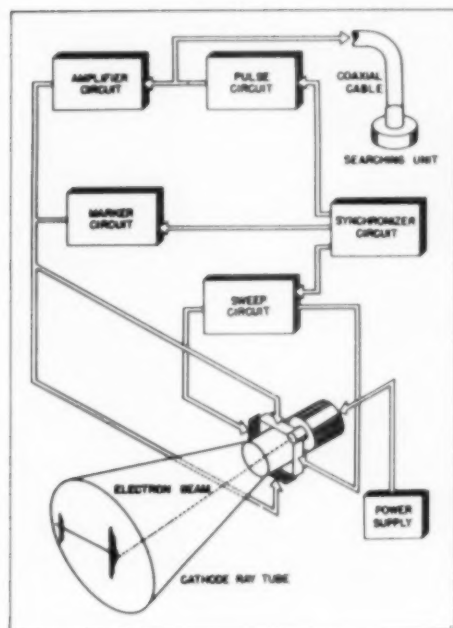


Fig. 2 (Mundt and Hughes). Electronic setup of ultrasonic Reflectoscope (taken from manual, *Ultrasonic Testing*, published by Sperry Products, Inc.).

screen to specific distances between the indications (fig. 1-A, B, and C). A marker circuit superimposes a scale on the horizontal sweep line of the cathode ray tube. For this work the marker circuit was set so that each deflection equals 10 mm. The Reflectoscope is shown in Figure 3, and the camera attachment, positioning device, and application of the searching unit to the patient's eye is illustrated in Figure 4. The diagram in Figure 5 illustrates the position of the crystal vibrator of the searching unit and reflections from the various surfaces of an eye containing a malignant melanoma of the choroid. The tube of the searching unit (fig. 5-A) is placed over the end. The saline solution acts as a transmission medium because ultrasonic waves of higher frequency do not pass through air. Originally the rubber membrane was placed in direct contact with the eye using methyl cellulose as a couplant. It

was found, however, that any slight movement of the searching unit or eye would cause a slight stretching or contraction of the rubber membrane. This, in turn, would cause spurious indications on the cathode ray tube. Also, the reflections from the anterior part of the globe were superimposed on those from the rubber membrane. For these reasons, the searching unit could not be used for any pathology located anteriorly in the eye. Consequently when working with patients, a plastic tube was placed over the lids, and this was filled with normal saline until the end of the searching unit became immersed.

The major reflecting surfaces are shown in Figure 5; namely, A, the rubber membrane on the end of the tube of the searching unit; B, the cornea; C, the iris and anterior surface of the lens; D, the posterior surface of the lens; E, the top of the tumor; and F, the posterior coats of the eye. A picture cannot be obtained which shows at the same time maximal indications from all the reflecting surfaces of the eye. The relative position of the searching unit to these surfaces is very important. For example, if the ultrasonic waves strike the anterior surface of the cornea perpendicularly to its tangent, a larger amount of the waves is reflected than if it strikes it at an angle. The more waves that are reflected, the higher will be the indications on the cathode ray tube. Consequently, large indications may be obtained from the cornea, the iris, the lens, or posterior coats of the eye depending on the position of the searching unit, but large, well-defined indications cannot be obtained from all of these surfaces at one time. To help in determining the source and character of the various reflections from the eye, isolated parts of a pig's eye were placed in a beaker of normal saline and studied.

There have been several reports that ultrasonic waves have caused the formation of corneal opacities and cataracts and the liquefaction of vitreous.³ The Reflectoscope gives an intermittent type of ultrasonics. If the

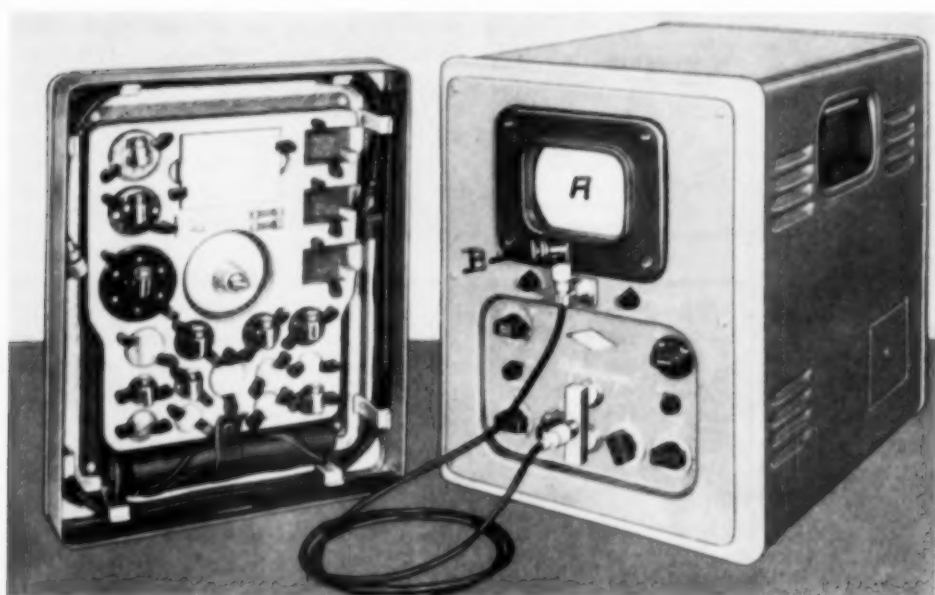


Fig. 3 (Mundt and Hughes). Type UR Reflectoscope equipped for double-searching unit testing and provided with a delayed sweep feature (taken from manual, *Ultrasonic Testing*, published by Sperry Products, Inc.). (A) Cathode-ray screen on which the ultrasonic reflections are projected. (B) Crystal vibrator or searching unit (transducer) which converts electric impulses into ultrasonic waves, and also receives the reflected "echoes" of the ultrasonic waves for transmission as electric impulses to the cathode ray tube.



Fig. 4 (Mundt and Hughes). (Left) Reflectoscope with camera attachment. (Center) Positioning device. (Right) Position of searching unit inside a plastic cylinder containing saline above the patient's eye.

searching unit is held on an eye for 20 minutes, the total exposure time of that eye to ultrasonic waves is less than one tenth of a second. The average power output for the crystal is less than one milliwatt per square centimeter. There is no focusing of the waves which would facilitate thermal corneal opacities, cataracts, or liquefaction of the vitreous. Rabbit eyes have been exposed for 20 minutes. Within an hour or so following exposure, the aqueous becomes fibrinous but this clears in a day or two. The rabbits have been followed now for over seven months and no corneal opacities, cataracts, or liquefaction of the vitreous have been observed. No adverse changes have been seen in humans on shorter exposure.

RESULTS

The ultrasonic tracings of two normal human eyes are shown in Figure 6. In both A and B the large reflections at the left are

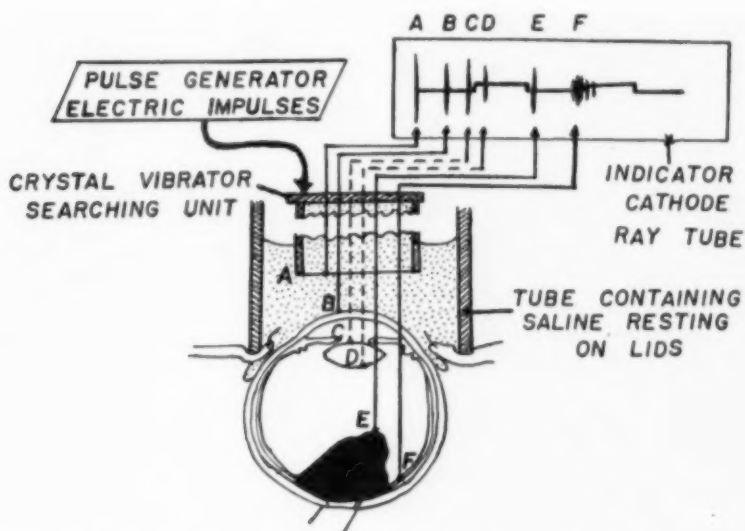


Fig. 5 (Mundt and Hughes). Diagram showing the position of the searching unit in relation to the eye, and the source of the reflecting surfaces as they appear on the indicator cathode ray screen.

from the rubber membrane of the searching unit. In A, there are three clearly demonstrated indications anteriorly. The first is the cornea, the second is the anterior surface of the iris and lens, and the third, the posterior surface of the lens. The reflections from the posterior coats of this eye are not as clearly separated as in the other normal eye shown

in B. Here the indications from the posterior coats of the eye are more distinct. There are four and occasionally five separate reflections from the posterior coats of the normal eye. The exact origin of each reflection is not clear. As mentioned previously, each segment of the horizontal base line equals 10 mm. In Figure 6, the distance from the beginning of the corneal indication to the

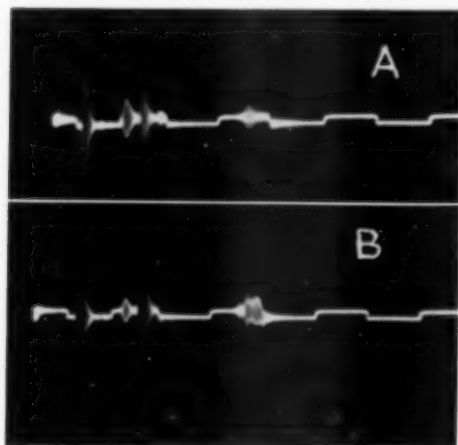


Fig. 6 (Mundt and Hughes). Ultrasonic tracings of two normal human eyes.

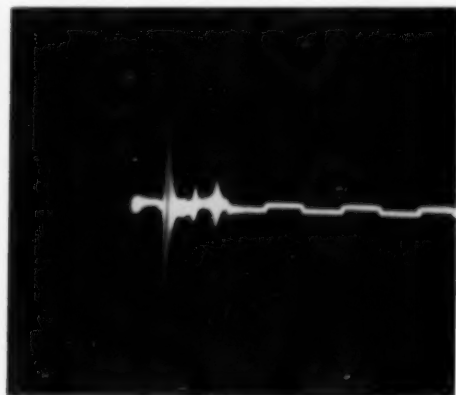


Fig. 7 (Mundt and Hughes). Ultrasonic tracing of a child's eye with microphthalmos and retrolental fibroplasia.

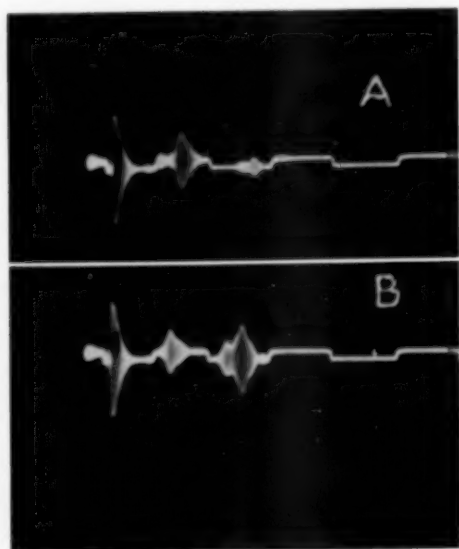


Fig. 8 (Mundt and Hughes). (A) Reflections from a normal enucleated pig's eye suspended in a beaker of saline. (B) Reflections from a pig's eye containing a three-mm. square piece of carcinoma of the breast in the suprachoroidal space posteriorly.

first reflection from the posterior coats of the eye is about 25 mm.

Figure 7 shows the recording of an eye of a child with microphthalmos and retrolental fibroplasia. It was made by our original method in which the rubber membrane was placed in direct contact with the cornea. The first large reflection is from the rubber membrane and cornea. The next clear reflection is from the retrolental membrane, and the third reflection on the right are the reflections from the posterior coats of the eye. The distance from the anterior reflection to the posterior reflection is about five mm. less in this microphthalmic eye than in a normal eye.

Small pieces of tumor removed from different parts of patients' bodies were placed in the suprachoroidal space of an enucleated pig's eye through an incision in the posterior part of the sclera. In Figure 8-A, the reflections from a normal enucleated pig's eye suspended in a beaker of saline are shown. Figure 8-B shows a pig's eye in which a

small piece of carcinoma of the breast has been implanted in the suprachoroidal space. The posterior reflections are closer to the anterior reflections and are larger than in the normal eye.

In Figure 9, A is a tracing of a normal pig eye and B is a pig eye in which a small piece of leiomyoma of the uterus was placed in the suprachoroidal space near the posterior pole. The distance from the cornea to the anterior part of the tumor in B is less than the distance from the cornea of the normal eye to the normal posterior reflections in A. The reflections from this benign tumor are much smaller than those from the carcinoma implant shown in Figure 8-B. This difference in the size of reflections from benign and malignant tumors is in agreement with the work of Wild and Reid.² The tumors were then suspended in a beaker of normal saline. Again, the reflections from the carcinoma (fig. 10-A) are larger than those from the leiomyoma (fig. 10-B). To demonstrate the capacity of the Reflectoscope to detect multi-

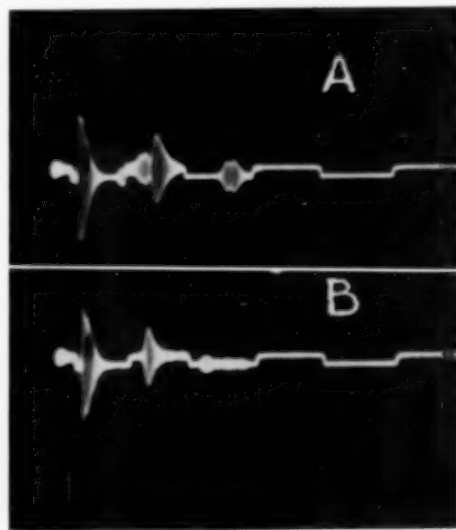


Fig. 9 (Mundt and Hughes). (A) Tracing of a normal pig eye. (B) Tracing of a pig eye in which a three-mm. square piece of leiomyoma of the uterus is present in the suprachoroidal space posteriorly.

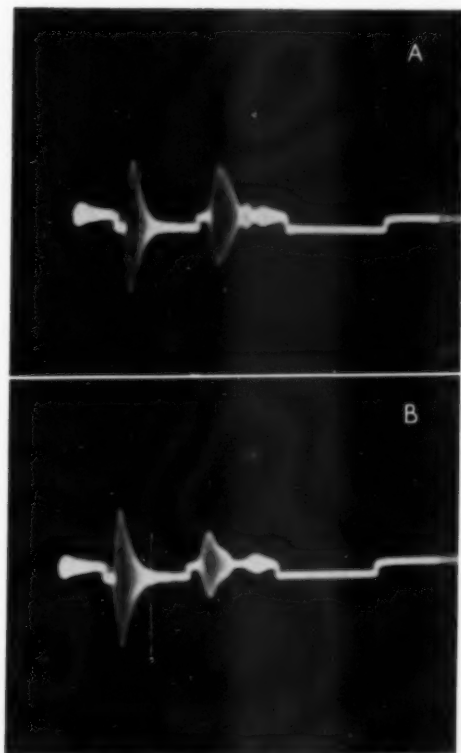


Fig. 10 (Mundt and Hughes). (A) Reflections from a piece of carcinoma of the breast suspended in normal saline. (B) Reflections from a piece of leiomyoma of the uterus suspended in normal saline.

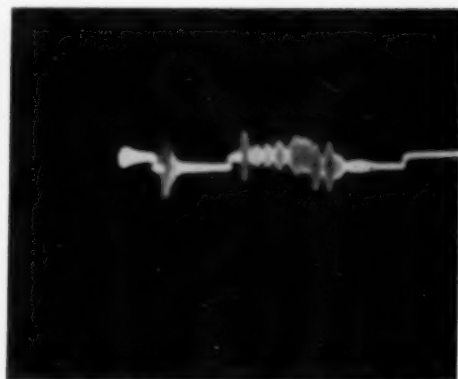


Fig. 12 (Mundt and Hughes). Multiple ultrasonic reflections from piece of breast tumor and fat illustrated in Figure 11.

ple discontinuities of surface, a piece of carcinoma of the breast with projecting ledges of tissue and overlying fat (fig. 11) was tested. In Figure 12 is shown how the several different surfaces of this tumor appeared in the ultrasonic tracing.

The studies were then directed to the detection of intraocular tumors in humans. Figure 13-A is the normal eye of a patient, and Figure 13-B, his other eye which contained a malignant melanoma near the posterior pole. In the normal eye the distance from the cornea to the beginning of the

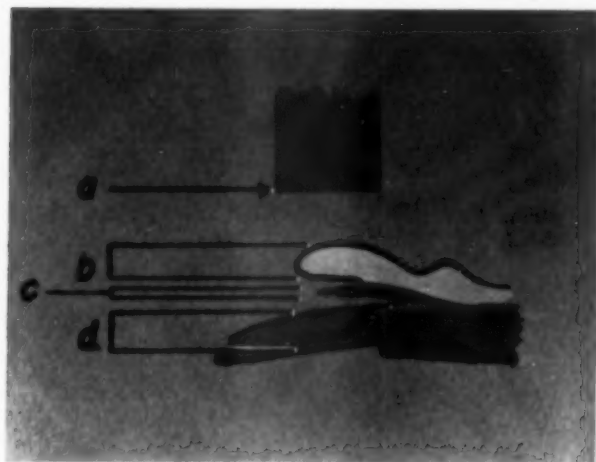


Fig. 11 (Mundt and Hughes). Diagram showing the various discontinuities of surface of a piece of carcinoma of the breast and fat. (a) Rubber membrane on end of searching unit of Reflectoscope. (b) Layer of fat. (c) Small ledge of tumor covered by capsule. (d) Thicker layer of carcinoma.

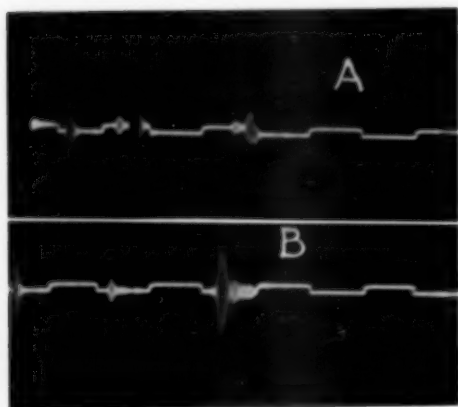


Fig. 13 (Mundt and Hughes) (A) Normal human eye. (B) Opposite eye of same patient containing a malignant melanoma near the posterior pole. Tracing taken before enucleation.

posterior reflections is about 25 mm. In B the distance from the cornea to the tumor is 20 mm. In B the posterior reflections are larger than in the normal eye.

In Figure 14 is shown the tumor. This eye before calotting was suspended in a beaker of normal saline and studied with the Reflectoscope.



Fig. 14 (Mundt and Hughes). Enucleated eye of patient whose tracing is shown in Figure 13-B. Diagnosis was malignant melanoma of the choroid.



Fig. 15 (Mundt and Hughes). Diagram showing different positions of the searching unit over the enucleated eye of the patient shown in Figures 13 and 14. This eye was suspended in saline before calotting. Position one represents the ultrasonic waves passing through the outer edge of the globe. Position two, Reflectoscope directly over the tumor. Position three, Reflectoscope directly over the cornea. Position four, Reflectoscope directly over the edge of the globe.

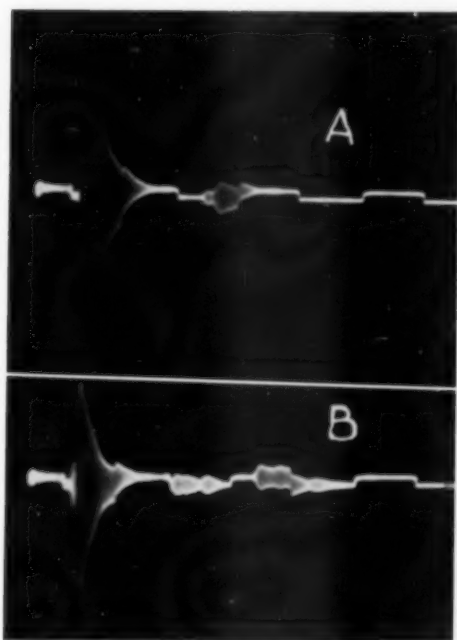


Fig. 16 (Mundt and Hughes). (A) Searching unit in position one Figure 15 directly over the edge of the globe. (B) Searching unit midway between positions one and two on Figure 15.

The diagram in Figure 15 shows how the searching unit was moved gradually across the eye while a series of photographs were obtained of the various ultrasonic tracings. In Figure 16-A, the searching unit was just over the edge of the globe. Consequently, there is no clearly separated anterior and posterior reflections, but only a single series of reflections which represent the outer edge of the coats of the eye. In Figure 16-B, the searching unit has been moved onto the globe a little farther, so that separate anterior and posterior reflections are found. In Figure 17-A, the reflections from the front part of the eye have moved more anteriorly, and some evidence of the tumor posteriorly is visible. In Figure 17-B, the searching unit is

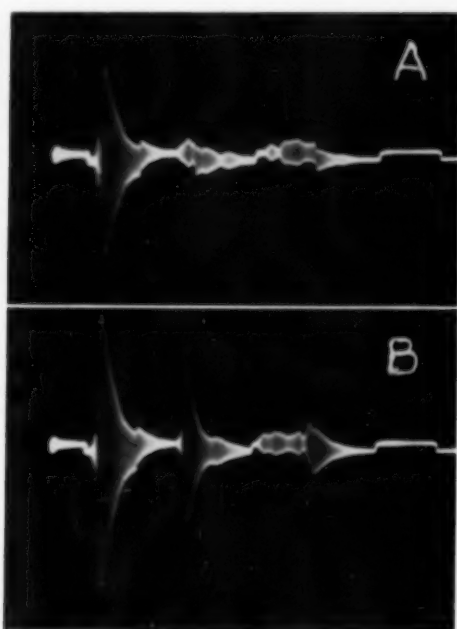


Fig. 17 (Mundt and Hughes). (A) Searching unit in position two of Figure 15. (B) Searching unit in position between two and three on Figure 15.

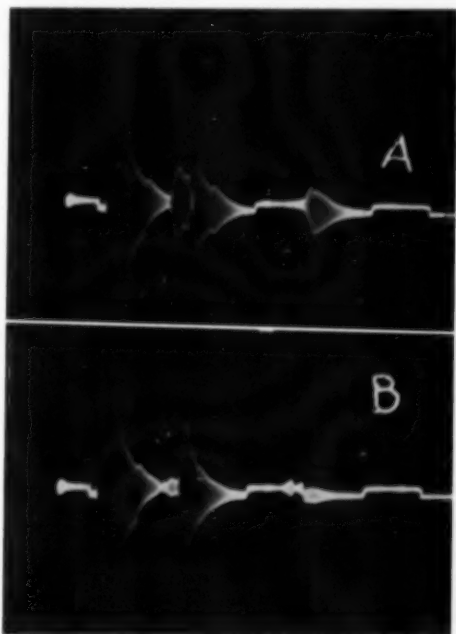


Fig. 18 (Mundt and Hughes). (A) Searching unit in position three of Figure 15. (B) Searching unit in position between three and four of Figure 15.

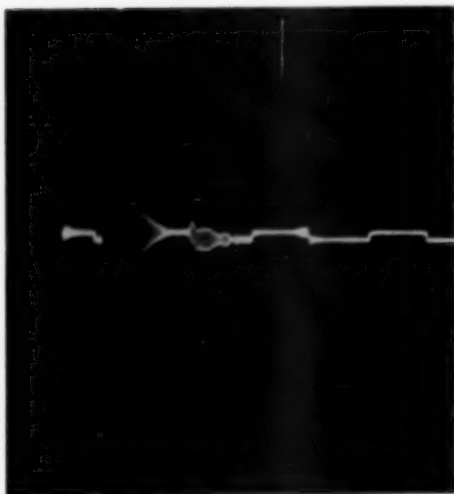


Fig. 19 (Mundt and Hughes). Searching unit in position four of Figure 15.

directly over the tumor. In Figure 18-A and B, tumor is no longer visible, and Figure 19 shows the tracing when the searching unit is just over the edge of the globe without clearly separated anterior and posterior reflections.

Figure 20-A is the normal eye of another patient. Figure 20-B is the opposite eye which contained a malignant melanoma near the posterior pole. Here again, the posterior

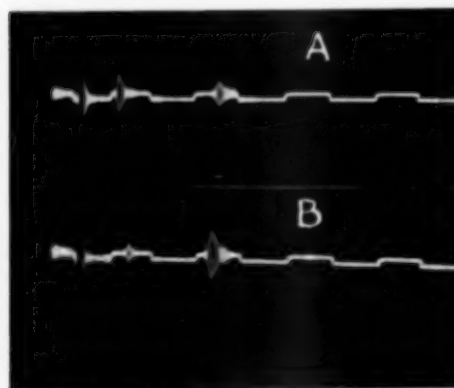


Fig. 20 (Mundt and Hughes). (A) Normal ultrasonic tracing of a normal eye. (B) Tracing of the opposite eye of the same patient which contained a malignant melanoma near the posterior pole.

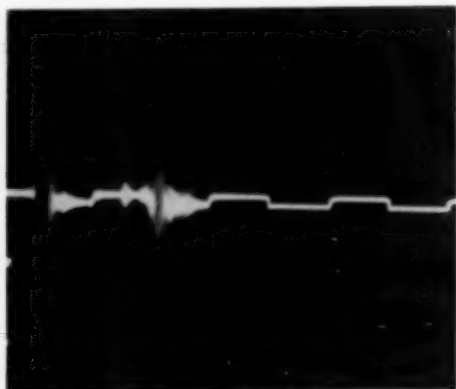


Fig. 21 (Mundt and Hughes). Ultrasonic tracing in which the rubber membrane of the searching unit was placed directly on the cornea. Lower photographic magnification than in previous pictures. This eye contained a malignant melanoma of the choroid.

reflections are larger and nearer the anterior ones in the normal eye. The pictures in Figures 21 and 22 were made with the original

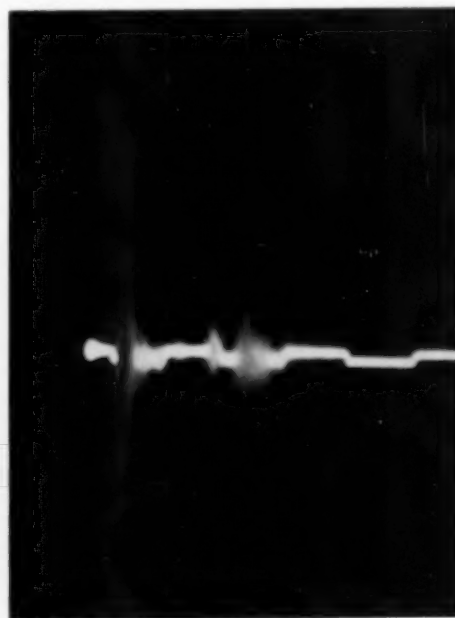


Fig. 22 (Mundt and Hughes). Another patient studied with the technique given in Figure 21, demonstrating a malignant melanoma posteriorly.

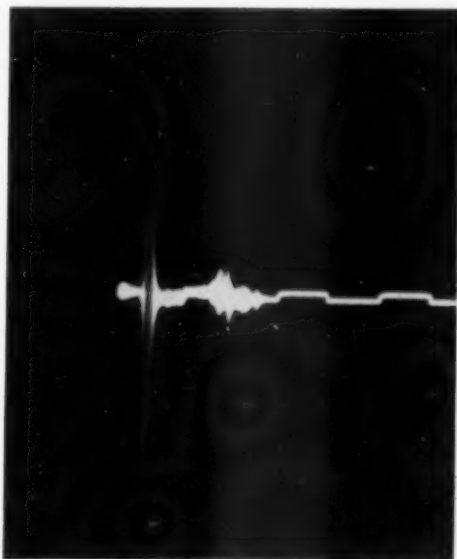


Fig. 23 (Mundt and Hughes). Ultrasonic tracing according to the technique outlined in Figure 21 of a child's eye containing a retinoblastoma.

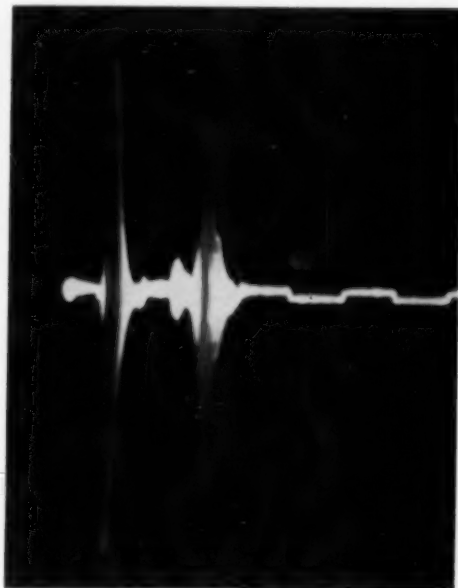


Fig. 24 (Mundt and Hughes). Ultrasonic tracing of another child's eye containing a retinoblastoma.

method in which the rubber membrane of the searching unit was placed directly on the cornea, and also less photographic magnification was obtained. They show eyes of two other patients which contained malignant melanomas. Here the distances from the beginning of the anterior reflections to the tumors are only about 15 mm. and 17 mm., respectively. The posterior reflections in Figure 21 are also larger than found in the normal eye.

Figure 23 shows the tracing of a child's eye which contained a retinoblastoma. Here the posterior reflections are large and multiple, and have extended anteriorly. Figure 24 is from another child with a retinoblastoma. The posterior reflections are tremendous and are displaced anteriorly. Both Figures 23 and 24 were taken with the original method in which the rubber membrane rested directly on the cornea.

The question arises whether a serous detachment of the retina can provide a new reflecting surface displaced anteriorly and therefore be confused with a tumor. Figure

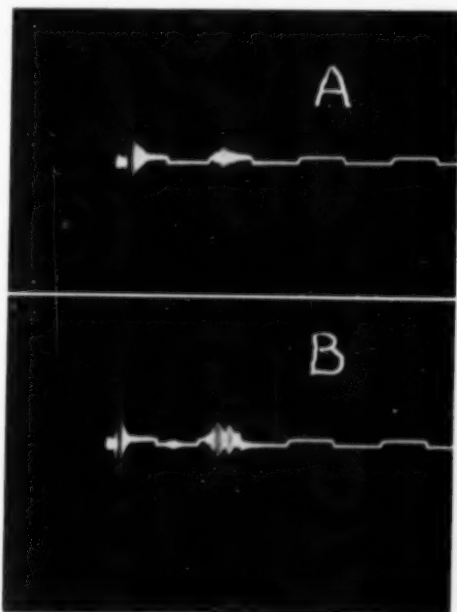


Fig. 25 (Mundt and Hughes). Ultrasonic tracing using technique outlined in Figure 21. (A) Normal eye. (B) Opposite eye containing a large retinal detachment.

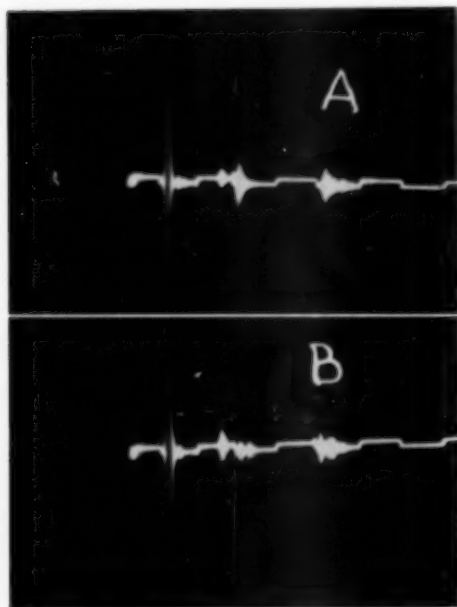


Fig. 26 (Mundt and Hughes). (A) Tracing of a normal eye. (B) Tracing of the opposite eye containing a large retinal detachment.

25-A shows the findings in the normal eye of a patient. Figure 25-B shows the findings in his opposite eye which contained a large retinal detachment. These studies were made using the original method. The distance from the anterior to the posterior reflections is about the same in both eyes. There is a

small indication on the base line about 10 mm. anterior to the posterior reflections in Figure 25-B. The amplitude is small. If it were a reflection from the detached retina, the 10 mm. anterior displacement would be equivalent to about 30 diopters of detachment, and this is much farther forward than the retina was in this case. We have occasionally found indications such as this in normal eyes. Figure 26-A shows the normal eye of another patient and Figure 26-B, his opposite eye which contained an almost complete retinal detachment. The two pictures are about the same.

CONCLUSIONS

This preliminary report is presented because the ultrasonic "Reflectoscope" appears to be a tool with which one is able to detect the distances of various reflecting surfaces of the eye from the cornea. At the present time this can be done with an accuracy not greater than one or possibly two millimeters. Simple serous detachments can probably be differentiated from those due to tumors with this instrument. It is unknown if tumors can be differentiated from such things as hemorrhages or scar tissue. The Reflectoscope also offers interesting possibilities in the diagnosis and localization of nonradiopaque foreign bodies.

1853 West Polk Street (12).

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WOUND HEALING OF THE IRIS*

IN THE PRESENCE OF AUTOLOGOUSLY TRANSPLANTED GRANULATION TISSUE

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In a previous publication,[†] two principal theories have been considered which might account for the lack of effective fibroblastosis commonly exhibited by the iris. First, much of the experimental evidence alluded to is consistent with a theory that the connective tissue of the adult iris stroma has no proliferative capacity. Secondly, it has appeared possible that the frequent failure of iris wounds to heal may be accounted for by a theory that local influences in the anterior chamber restrain the proliferation of intracameral connective tissue.

The work to be described represents an effort to test further the validity or mutual importance of these two theories.

The reasoning supporting the plan of the experiments to be described is as follows:

If it is true that the first theory is correct, that iris tissue lacks the capacity to proliferate, this lack should be demonstrable for this tissue removed to extraocular locations, and, conversely, connective tissue of extraocular origin should be capable of proliferation within the eye, given an adequate stimulus. If, on the other hand, the second theory is correct, that conditions within the anterior chamber suppress the reproduction of connective tissue elements, then connective tissue cells of extraocular origin should exhibit the effects of this suppression just as do connective tissue cells of intraocular origin. Conversely, if the intraocular climate suppresses the reproduction of intraocular connective tissue elements, then these elements, if re-

moved to another climate, should exhibit the capacity to proliferate, given an adequate stimulus.

This report deals with observations on the behavior of connective tissue of autologous subcutaneous origin when transplanted to the anterior chamber in the presence of injuries to the iris produced by diathermy burns. Such connective tissue is observed to be hardly more effective in causing fibrosis of these burns than is the iris itself.

Previous experience[‡] has indicated that it is possible to produce standard focal burns of the iris with ordinary clinical diathermy apparatus, and these observations serve as controls for the present experiments. Such burns when examined histologically after two or three days showed a necrotic edematous focal lesion, rapidly invaded by blood vessels, but exciting little or no fibroblastosis; the eventual fate of the necrotized area was atrophy without organization, often leaving iris holes or colobomas.

The behavior of granulation tissue of subcutaneous origin, elicited by buried foreign bodies of polyethylene, when transplanted to the anterior chamber, has also been studied. This transplanted granulation tissue appeared to "take" on anterior chamber transplantation. It became vascularized from the iris or cornea or both. Its appearance on histologic examination showed it to be healthy, but ultimately it shrank and atrophied without producing noticeable amounts of collagen.

MATERIALS AND METHODS

Young adult guinea pigs were used exclusively for these experiments. Granulation tissue was obtained by the use of foreign bodies of polyethylene plastic. These were of two forms. Short lengths of about one

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† Snell, A. C., Jr.: Reactions of the iris to injury. *Tr. Am. Ophth. Soc.*, 1955, In press.

mm. of No.-90 polyethylene tubing were cut, creating collars or doughnutlike pieces. Also flat pieces of polyethylene film were cut roughly circular, 1.5 mm. in diameter, and multiple perforations were made in these with a needle point, creating a rough sieve. Both of these kinds of foreign bodies were introduced into the subcutaneous tissues of guinea pigs and were found to become filled and surrounded by granulation tissue including many macrophages and foreign-body giant cells, blood vessels, and large numbers of fibroblasts which began to produce collagen in a few days (fig. 1).

Seven or eight days after the subcutaneous introduction of the foreign bodies, the animals were again anesthetized by intraperitoneal injections of nembutal, and the foreign bodies were retrieved through skin incisions after shaving and washing. Before excising the foreign body from the subcutaneous area, both eyes of each animal were opened by keratome incisions into the anterior chambers. Each foreign body was grasped by forceps, its attachments to the subcutaneous tissues were trimmed with scissors, and without further manipulation or transfer to any solution the foreign body

with its envelope and core of granulation tissue was transferred to the anterior chamber. Each eye received one foreign body placed between iris and cornea in the quadrant farthest removed from the corneal incision. The skin incisions were closed with silk or skin clips, but no suturing of the corneal wounds was necessary.

The granulation tissue transplanted in this manner to the anterior chamber usually appeared to take and to become vascularized more consistently if it was transferred along with the foreign body which had evoked it in the subcutaneous tissues. Often this transplanted material became quite pink after three or four days, and even when it did not appear grossly vascularized, microscopic study revealed healthy looking tissue (fig. 2). However, several of these transplants appeared quite inert, white, and unhealthy; others were associated with purulent reactions, and eyes with these kinds of reactions were discarded from the experiment.

If the transplants were allowed to remain unmolested in the anterior chambers, their fate was eventually to fade and atrophy. The foreign bodies in part became cleared of their envelope of connective tissue, although for-

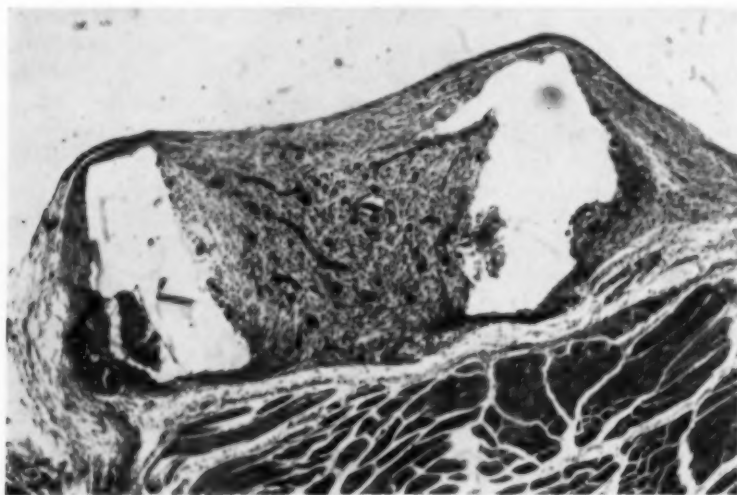


Fig. 1 (Snell). Foreign-body reaction in subcutaneous tissues of guinea pigs.



Fig. 2 (Snell). Granulation tissue of subcutaneous origin four days after transplantation to the anterior chamber.

eign-body giant cells seemed to persist almost indefinitely. Various degrees of adhesions between iris, cornea, and foreign body also persisted. There usually remained a collection of fibrocytes with a spindle of collagen fibers on the posterior surface of the cornea in the region of the transplant and foreign body.

On the third, fourth, or fifth day after transplantation, suitable eyes received diathermy burns of the iris. The animals were anesthetized a third time and the corneal wound reopened with a spatula. Standard clinical diathermy apparatus was used to produce focal burns of the irises, using a glass-insulated electrode with exposed tip. These burns were made as close as possible to, or exactly at, the site of the transplanted granulation tissue and foreign body, and were made from the under surface of the iris, with the electrode tip directed anteriorly.

The subsequent behavior of these injuries was followed by periodic observation of the living animals with the slitlamp and corneal microscope. At various intervals the animals were killed, the eyes were removed immediately and fixed in Zenker's solution.

Each specimen was blocked to include the area of the transplant and injury, imbedded in paraffin, and sectioned serially. Standard hematoxylin and eosin stains were used throughout.

RESULTS

It had been expected that a large number of guinea pig eyes could be treated as already described, sufficient to provide data that would have statistical meaning. However, the total procedure proved to be most inefficient in this respect. While 46 guinea pigs were originally included in the experiment, 63 eyes were found to be meaningless because of animal mortality, purulent reactions, excessive operative trauma, or failure of the transplanted tissues to take. Of the 29 eyes in which apparent technical success was achieved, 11 exhibited no gross or microscopic evidence of injury to the iris. This is an important negative. It cannot be interpreted as healing of the iris injury but rather as failure to produce injury, probably due to insufficient application of diathermy current. In four of the remaining 18 eyes, obvious injuries were produced so far removed from

the site of the transplanted granulation tissue that the injured area cannot be considered to have been influenced by the transplant. This leaves only 14 eyes in which the planned experiment was successfully carried out; that is, the production of focal injuries of the iris in the immediate neighborhood of healthy transplanted fibroblasts of subcutaneous origin.

In 12 instances the area of iris injury clearly escaped organization by the neighboring transplanted fibrous tissue. No evidence of infiltration of the original necrotic portion of iris took place. In the living animal iris holes or colobomas were seen to appear at the site of the iris burn even when this was overlapped by the transplanted granulation tissue.

Figure 3 illustrates a portion of atrophic iris 29 days after injury. The injured portion of iris lies posterior to a perforated disc of polyethylene film, and is bounded medially and along its posterior surface by a strip of fibrous tissue. This fibrous tissue has failed to invade, to any significant degree, the area of injury to the iris, which is evidently absorbing.

In Figure 4, also made 29 days after in-

jury, much of the transplanted granulation tissue lying on the posterior surface of the perforated film has absorbed and has failed to invade or organize an iris burn at this region. The injured portion of iris has largely absorbed.

Figure 5 represents a guinea pig eye removed 48 days after diathermy burn to the iris. The site of the burn is marked by rounded clumps of pigment; this pigment was freed by the injury and taken up by phagocytes. In spite of the fact that blood vessels course through the region of injury, no fibrous tissue organization has occurred. However, fibrous tissue is directly available to the zone of injury, and can be seen lying in a spindle along the posterior surface of the cornea. The iris, the foreign body, the cornea, and the spindle of fibrous tissue are mutually adherent, yet the zone of injury fails to exhibit connective tissue organization.

In Figure 6 the zone of iris injury extends on both sides of the transplanted granulation tissue. The damaged and atrophic tip of iris on the right connects with the fibrous plug by a delicate extension of what may be iris surface endothelium, and on the left a

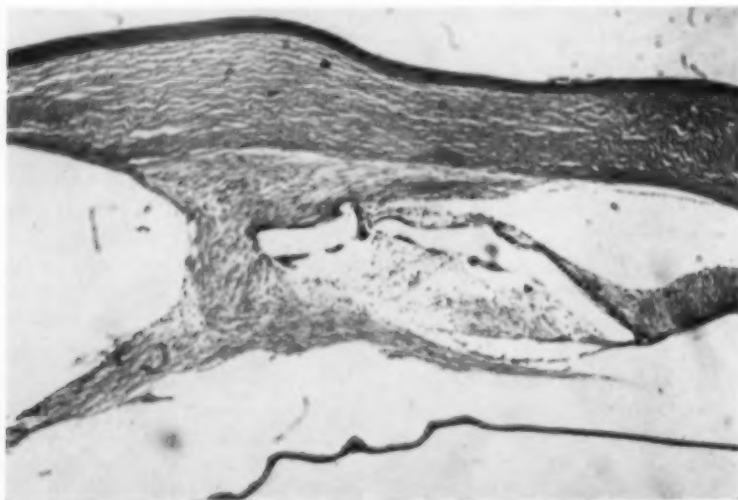


Fig. 3 (Snell). Atrophic iris, 29 days after injury, has escaped organization by underlying fibrous tissue.

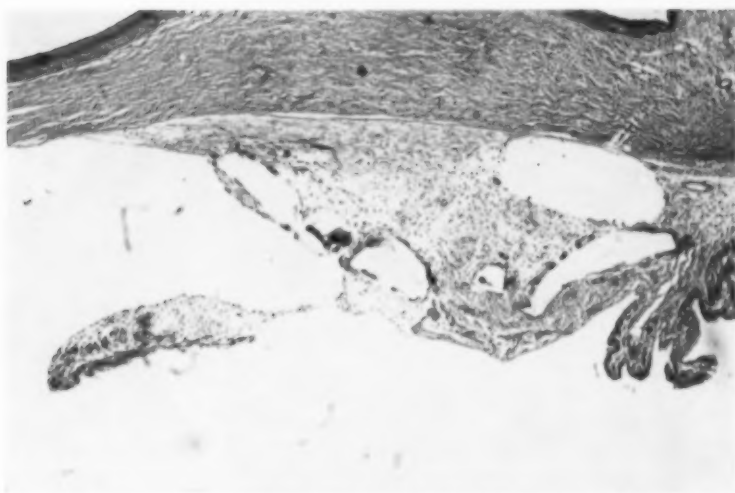


Fig. 4 (Snell). Iris defect and atrophy adjacent to foreign body, 29 days after injury.

complete iris hole is present, 52 days after injury.

A certain variation from the pattern illustrated in Figure 6 is shown in Figure 7. Underlying the transplanted foreign body and granulation tissue, part of the iris is absent and appears to be replaced by a layer of connective tissue which fans out from the core

of the collar-shaped foreign body. However, it is evident that this connective tissue has failed to unite with the opposite margin of the iris burn and a hole in the iris has appeared. Observation of the living animal and serial sections of the specimen confirm that this defect is not in the zone of the pupil.

In the two other eyes, removed eight days

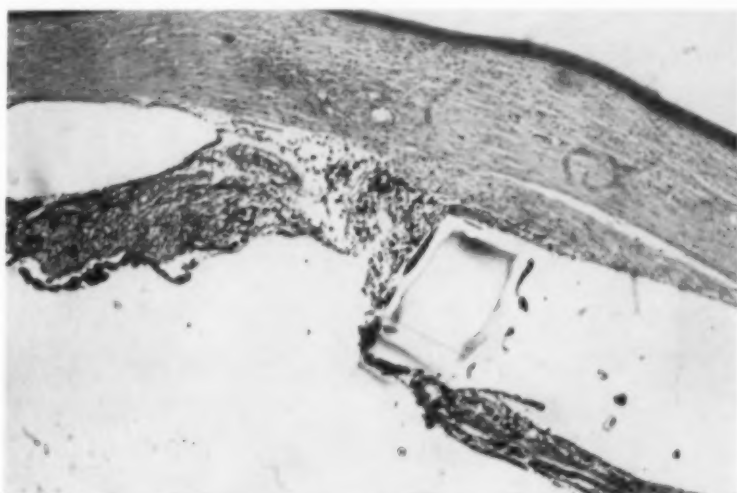


Fig. 5 (Snell). Pigment clumping and vascularization in zone of iris injury without invasion by adjacent connective tissue, 48 days after injury.



Fig. 6 (Snell). The zone of iris injury extends on both sides of the transplanted granulation tissue.

after injury, the area of necrotized iris appeared to be encapsulated by active connective tissue. This connective tissue, however, gave no evidence of uniting with the peripheral margin of the region of injury, so that the ultimate result would be expected to be a separation of the margin of the injury from what was originally a closely approximated bundle of fibroblasts.

DISCUSSION

The evidence presented has the serious limitation that the experiment was so frequently a failure from the technical standpoint. On the other hand, in those instances in which technical success was achieved, the pattern appears to be unmistakably clear; healthy transplanted granulation tissue of subcutaneous origin failed to provide effec-



Fig. 7 (Snell). Failure of margin of zone of iris injury to remain united to fibrous tissue underlying foreign body.

tive fibrosis for the healing of the iris burns. Philosophically, one may wonder if fibroblasts of distant, although autologous origin should be expected to be capable of healing an alien organ. No control is offered to test the truth of such a possibility, except that general opinion among cytologists and pathologists apparently assigns no regional specificity to fibroblasts of connective tissue origin.

If it can be expected that this type of experiment has meaning, then it must be concluded that something in the environment of the anterior segment of the guinea pig eye interferes with effective fibrosis; either in the sense that proliferation is inhibited, or in the sense that cohesion is inhibited. It is felt that the evidence suggests the existence of influences operating in the anterior chamber which inhibit or suppress or modify the behavior of fibroblasts transplanted to the an-

terior chamber, reducing the extent of fibrosis which would otherwise be expected. It is postulated that the same influences may modify the behavior of connective tissue cells of local origin, and may be responsible, at least in part, for the common failure of iris wounds to heal by fibrosis.

SUMMARY

Connective tissue cells of granulation tissue of subcutaneous origin, when transplanted to the anterior chamber, are observed to be as ineffective in producing fibrosis of diathermy burns of the iris as are the connective tissue cells of the iris itself. It is believed that this observation gives support to the concept that the failure of iris wounds to heal by fibrosis may be due to inhibitory influences present in the anterior chamber.

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SUCCESSFUL TRANSPLANTATION OF A FROZEN HUMAN CORNEA*

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Until recently all attempts to transplant human corneas preserved by freezing have been disappointing. In rats, Weiss and Taylor¹ reported success in using frozen corneal transplants but, in rabbits, attempts by others using similar methods have been unsuccessful. Smelser and Ozanics² believed that in the rabbit the grafts become cloudy because the cells did not survive freezing.

In recent years various types of cells have been preserved by freezing. One widely used technique has been to freeze cells in glycerol solutions. Polge³ first demonstrated that spermatozoa could be frozen without loss of function. Hollander and Nell⁴ have shown

that bacteria also remain viable after repeated freezing and thawing in the presence of glycerol. It seemed plausible that corneal cells would also remain viable if frozen, using this technique. Eastcott, Cross, Leigh, and North, employing a similar technique, successfully transplanted human cornea both in lamellar and penetrating grafts.⁵

Histologic examination of rabbit corneas which were frozen and thawed in normal saline solution revealed narrowing of the epithelial layer and distortion of the individual nuclei as though the tissue had been crushed. Examination of rabbit corneas which had been frozen and thawed as many as four times in normal saline to which glycerol had been added showed well preserved epithelium, essentially similar to that of normal unfrozen corneas.

As a check on the viability of the corneas after freezing, the dehydrogenase activity

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was examined as follows. The resected anterior portion of the right eyes of eight rabbits were placed in saline, and that of the left in saline with glycerol. These were frozen and thawed up to four times and then transferred to a solution of a tetrazolium salt, after which the tissues were incubated at 37° C. In the presence of succinic dehydrogenase the tetrazolium salt is reduced to a blue-colored formazan.

The unfrozen corneas whether in saline or in saline-glycerol, and the corneas in saline glycerol after freezing once, twice or four times, all developed the blue color. On the contrary, the corneas in normal salines, when frozen once, twice, or four times, showed a successively decreasing amount of color. On the basis of this indication, that the glycerol frozen material was still viable after freezing and thawing, together with the observation of Eastcott, Cross, Leigh, and North,⁵ the following application of this technique was undertaken.

CASE REPORT

A patient (J. M.) who had had bilateral eight-mm. corneal grafts for extreme keratoconus was seen on June 15, 1954, with a cloudy graft and a bullous keratitis of the left eye. Vision was reduced in this eye to counting fingers at one foot, and in the right eye 20/40+.

A fresh whole cornea was placed in 10 ml.

of 15-percent glycerol in saline frozen at minus 70°C., kept at this temperature for one and one-half hours, and then thawed at a temperature of 37°C. The cornea, with the epithelial side down, was pinned to a cork, and an eight-mm. full thickness trephine plug was carefully prepared. The plug was sutured in the recipient's cornea with 16 direct silk sutures.

Healing was uneventful with the exception of a synechia at the 5-o'clock position. In spite of this the graft has remained clear for 17 postoperative months (last examination November 18, 1955), with a vision of 20/30 corrected to 20/20 with a +2.0D. sph. -2.25D. cyl. ax. 110°.

SUMMARY

1. Evidence based on histologic examination, and succinic dehydrogenase activity measurement, suggests that damage consequent to freezing corneas is minimal when the tissue is frozen in glycerol solution.

2. A human cornea was frozen and used as a graft after having been frozen for one and one half hours. The graft has remained clear for 17 postoperative months with a corrected vision of 20/20.

3. The work of Eastcott and others demonstrating that frozen corneas are practical for transplantation is confirmed.

Johns Hopkins Hospital (5).

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RADIOACTIVE PHOSPHORUS FOR THE DETECTION OF INTRAOCULAR TUMORS*

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The diagnosis of an intraocular neoplasm is sometimes uncertain and the decision to remove an eye for a suspected tumor is often one of the major tests of an ophthalmologist's judgement. Because radioactive phosphorus might be of value in solving these problems, studies have been made of the radioactivity over both normal and abnormal eyes following the intravenous injection of radioactive phosphorus. Thomas et al.,¹⁻³ Dunphy et al.,⁴⁻⁷ Eisenberg et al.,^{8,9} and Bettman et al.¹⁰ have previously reported their experience with radioactive phosphorus in the detection of intraocular tumors. In this paper a report is given of the experience obtained at Walter Reed Army Hospital with this method.

The emanations from radioactive phosphorus are beta particles, while those from radioactive iodine are mainly gamma irradiations. As was to be expected, the attempts by Trevor-Roper et al.¹¹ to detect intraocular neoplasms using the gamma-emitting radioactive di-iodofluorescein were not successful because the deeply penetrating gamma irradiations set off from the surrounding nonocular tissues were easily detected by the counter. This obscured any ocular lesion that might have been present. However the fact that radioactive phosphorus is a beta emitter gives it a distinct advantage for use in ocular lesions. Because of the limited penetration of the beta particles from radioactive phosphorus, no masking scatter from the surrounding nonocular tissue is detected by the counter. Yet the beta ray's average penetration is sufficient to traverse the choroid and sclera and be detected easily by the counter

held against the eye, thereby revealing the state of the ocular tissues without interference by emanations from surrounding non-ocular tissues.

Living cells with high metabolic activity concentrate radioactive phosphorus more readily than do those with low metabolic activity.¹² Thus it has been found that osteogenic sarcoma cells show 12 times the concentration of radioactive phosphorus as do normal bone cells.¹³ Similarly areas of melanomatous skin show larger concentrations of radioactive phosphorus than nearby areas of normal skin.¹⁴ The metabolically active crystalline lenses from young rabbits concentrate more radioactive phosphorus than do the relatively inactive lenses from older rabbits.¹⁵ Likewise the lens epithelium has a much greater ability to metabolize radioactive phosphorus than the relatively inert lens fibers.¹⁶ In addition, the *in vitro* uptake of radioactive phosphorus by the lens is inhibited when metabolic poisons such as mono-iodo-acetate and cyanate are administered.

Intraocular tumors may be detected not only by the concentration of radioactive phosphorus due to the increased metabolic activity of their neoplastic cells, but, in addition, may be detected by the absolute increase in tissue mass that occurs with neoplastic growth within the hollow spherical globe.

METHOD

The radioactivity of P³² can be determined by making counts with a Geiger-Müller probe counter. The counting tube used in this study is the same one as described by Thomas et al.¹ It is encased in a small metal holder open at one end. A small mica window six mm. in diameter covers the opening. Only

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those beta particles that strike the mica window can be counted by the tube since the metal holder shields the counting tube in all other directions. In this way the counter "sees" only an area six mm. in diameter when it is held in direct contact perpendicular to the sclera. The counter is connected to a scaler with an automatic timing device which permits the direct reading from the scaler of the number of counts registered during some preselected time interval.

In our routine test for the detection of an intraocular neoplasm, a tracer dose of radioactive phosphorus is administered intravenously in the form of sodium phosphate* in isotonic saline. Total doses which have given satisfactory results in adult patients have varied in amount from 350 to 500 mc. In children satisfactory results have been obtained after doses of five mc. per kg. of body weight. The counts over the eye are made approximately 24 hours following the injection. After each eye has been anesthetized with tetracaine 0.5-percent solution, the probe counter is placed in contact with the conjunctiva over the sclera. It is important to hold the probe perpendicular to the tangent at the point of contact with the sclera. Usually it is difficult to take counts for longer than one minute as the patient cannot keep his eye immobilized for a longer time.

The scleral surface of each eye is mapped by recording on a chart the number of counts registered per minute when the Geiger-Müller counter is held in contact with the conjunctiva at different anatomic positions. Particular attention is given to the region known to overlie the intraocular lesion where a search is made for the area of greatest radioactivity. After the position of highest counting rate has been located, four or more one-minute counts are obtained at that position, and their mean computed. This figure represents the activity determined over the intraocular lesion. This mean count over the

intraocular lesion is then compared with a normal reference count. The best reference count is obtained from the opposite normal eye at the corresponding anatomic site where the mean count was obtained over the intraocular lesion. For the reference count the mean of at least four one-minute counts should also be used. For comparison of the activity over the intraocular lesion to the corresponding reference point in the normal eye, the ratio is computed of the mean activity over the lesion to the mean activity over the corresponding location in the normal eye.[†]

When an *in vivo* measurement is followed by enucleation, the entire external surface of the enucleated eye is mapped in a manner similar to that used prior to surgery. After the area of maximum activity is located, the mean of four or more one-minute counts is obtained over this position. For comparison, the mean of a like number of one-minute counts is obtained from that position on the sclera of the enucleated eye farthest removed from the area of maximum activity. After the eye is sectioned, counts are obtained directly over the intraocular lesions for comparison with those obtained from the surface of the globe before sectioning.

RELIABILITY OF SUCCESSIVE ONE-MINUTE COUNTS

Successive one-minute counts made *in vivo* will vary from each other even though they have been made in the same location on a single normal eye. It is necessary to know the amount of this normal statistical variation to interpret properly the counts obtained over intraocular lesions. A count over a lesion must exceed the normal variation to indicate the presence of an area of abnormal concentration of radioactivity.

To assess this variation, the reproducibility of counts was first studied *in vitro*. The eye

* The sodium phosphate (P^{32}) solutions were obtained from Abbott Laboratories, North Chicago, Illinois.

[†] Before this procedure was standardized, in a few of the earlier cases in this study, the radioactivity in the area of the lesion and the corresponding reference area were calculated on the basis of less than four one-minute counts.

probe counter and the automatic scaler were used. Counts were taken from a glass flask containing an aqueous solution of radioactive phosphorus in the form of sodium phosphate. The concentration had been adjusted to give a count within the range usually encountered clinically. Ten successive one-minute counts were made. The ratio of the highest to the lowest count was 1.33.*

The variation of successive one-minute counts was then studied *in vivo*. Sixty-seven pairs of counts were made from different locations in 25 normal eyes. Each of the two successive counts in a given pair was taken from the same location in a single normal eye. For each of the 67 pairs, a ratio was computed by dividing the higher count by the lower count. The variation observed in this ratio in the 67 pairs of determinations is shown in Table 1. In most cases the higher count was less than 50 percent larger than the lower count giving a ratio of less than 1.50. In only four of the pairs did the higher count exceed the lower one by more than 50 percent or a ratio of 1.50 or more. In view of this observed variability both *in vitro* and *in vivo*, we have considered as a positive test, highly suggestive of the presence of a tumor, only those cases where the count over the lesion was 50 percent greater than the count over the normal reference area.

ANALYSIS OF CASES

In this paper we are reporting the results obtained in studying 28 individuals at the Walter Reed Army Hospital. Two of the patients had generalized metastases from skin melanomas but no ocular lesions. In these patients, when the counter was placed over an area of melanoma, the count obtained was higher than that obtained from adjacent areas of skin free of melanoma. In one patient who had a chronic orbital fibromyositis no increased concentration of radioactivity could be found. Another patient had

TABLE 1
RELIABILITY OF SUCCESSIVE ONE-MINUTE COUNTS

Ratio Higher to Lower Count	Number
1.00-1.09	20
1.10-1.19	13
1.20-1.29	15
1.30-1.39	8
1.40-1.49	7
1.50 and over*	4
Total	64†

* Ratios of 1.60, 1.70, 1.73, 1.75.

† From 25 normal eyes.

a marked increase in the retinal vascular bed of one eye due to a congenital retinal arteriovenous anastomosis. In this patient there was no increased radioactivity over the abnormal eye in spite of the increased vascularity.

The remaining 24 patients had localized intraocular lesions. In these patients the test with radioactive phosphorus was successful in differentiating between neoplastic and non-neoplastic lesions when the lesion was situated anteriorly in positions accessible to the Geiger probe counter. However, when the lesion was posterior and out of reach of the Geiger probe counter, the method was not helpful.

Table 2 is a summary of the results obtained in anterior neoplasms. In most of the cases the count over the tumor was more than twice that over the corresponding area in the normal eye. In one instance the ratio was 1.49 when determined before enucleation. In this case the main portion of the tumor could not be reached by the probe before enucleation. However, after enucleation, the count ratio rose to 1.64 when the probe counter could be placed directly over the tumor. Seven of these anterior neoplasms were melanomas of the choroid, and two were retinoblastomas.

The count ratios for anterior non-neoplastic lesions are shown in Table 3. In these six cases the count ratios were all less than 1.50. Two of the cases were Coats' disease, two were fluid detachments of the retina, one

* Mean 151.6 cpm. Range 131-174 cpm. Standard deviation 12.4 cpm. Average deviation 9.8 cpm.

TABLE 2
RADIOACTIVITY IN ANTERIOR NEOPLASMS

Case No.	Ratio*		Remarks	Diagnoses†
	Before Enucleation	After		
19	3.83		Enucleation	Melanoma choroid, C-P
12	3.42		Enucleation	Retinoblastoma, C-P
14	3.24		Enucleation	Melanoma choroid, C-P
24	2.76		Enucleation	Melanoma choroid, C-P
13	2.38		Enucleation	Melanoma choroid, C-P
8	2.30	6.27	Enucleation	Melanoma choroid, C-P
27	2.12	4.39	Enucleation	Melanoma choroid, C-P
9	2.03	3.97	Enucleation	Retinoblastoma, C-P
22	1.49	1.64	Enucleation	Melanoma choroid, C-P

* Counts per minute over lesion divided by counts per minute over normal tissue.

† Clinical—C; pathologic—P.

an organizing vitreous hemorrhage, and one was a case of uveitis and glaucoma secondary to retained intraocular glass foreign bodies.

The count ratios for eight posterior lesions are shown in Table 4. In each of these posterior lesions the count ratios were less than 1.50 and the test did not separate neoplastic from non-neoplastic lesions. In Case 5 a count was made after enucleation, when the Geiger probe counter could be brought directly over the posteriorly located melanoma of the choroid. Although the count ratio before enucleation did not indicate a concentration of radioactivity, the count ratio after enucleation was 2.82 showing that this melanoma might have been detected clinically, if a suitable probe had been available for searching the posterior portions of the globe. Probes designed for this purpose are now being constructed,^{17, 18} but up to the

time of preparation of this paper, we have not had an opportunity to test them at Walter Reed Army Hospital.

In Case 6 the clinical diagnosis was melanoma of the choroid. Since the lesion was located posteriorly, the negative test with radioactive phosphorus was discounted and an enucleation was performed. After enucleation the globe was surveyed with the Geiger counter, and again no significant area of concentration could be found, this time even the counter was placed directly over the lesion after the globe had been sectioned. Pathologic examination showed that the lesion was an hemangioma of the choroid. Apparently there had not been sufficient growth of new tissue in the hemangioma to produce an area of increased radioactivity, nor had the increased quantity of blood been sufficient to give a significantly higher count.

TABLE 3
RADIOACTIVITY IN ANTERIOR NON-NEOPLASTIC LESIONS

Case No.	Ratio*		Remarks	Diagnoses†
	Before Enucleation	After		
2	1.43		No procedure	Coats' disease—C
21	1.35		Retinopexy	Fluid detachment—C-S
11	1.30		Enucleation	Retained glass foreign body—P
17	1.26		No procedure	Organizing massive hemorrhage—C
26	1.20		No procedure	Coats' disease—C
25	1.06		No procedure	Fluid detachment—C

* Counts per minute over lesion divided by counts per minute over normal tissue.

† Clinical—C, pathologic—P, surgical—S.

TABLE 4
 RADIOACTIVITY IN POSTERIOR LESIONS

Case No.	Ratio*		Remarks	Diagnoses†
	Before Enucleation	After		
18	1.42		No procedure	Metastatic chorioepithelioma—S
	1.39			
16	1.41		Enucleation	Melanoma choroid—C, P
15	1.27		No procedure	Angiomatosis—C
20	1.15		No procedure	Angiomatosis—C
23	1.05		No procedure	Disciform degeneration—C
6	0.97	0.84	Enucleation	Melanoma choroid—C
				Hemangioma choroid—P
5	0.85	2.82	Enucleation	Melanoma choroid—C, P

* Counts per minute over lesion divided by counts per minute over normal tissue.

† Clinical—C, pathologic—P, surgical—S.

COMMENT

From a review of our experience and reports in the literature, there is agreement that radioactive phosphorus is useful in detecting anterior neoplasms with the presently available Geiger probe counters. Perhaps with newly designed probes to explore the globe posteriorly, neoplastic lesions in that region may be detected. There is still some difference of opinion on several questions concerning the technique. One of these is the proper time to make counts from the eye following the injection of radioactive phosphorus. The other is the choice of the area to be used for the reference count.

In the early studies reported in the literature, counts were made over the eye within one to two hours following the intravenous injection of radioactive phosphorus. However, Dreisler,¹⁸ Corrigan,²⁰ and Bettman¹⁹ suggested that counts be made 24 hours or several days following injection. Counts made at this time might not only show less variation in normal eyes, but also give a greater difference between neoplastic and non-neoplastic areas. Counts made immediately following intravenous injection are likely to be largely the result of radioactive phosphorus in the blood stream. They would be indicative chiefly of the vascularity of the lesion. A longer time is required for the radioactive phosphorus to be metabolized and incorporated into the tissue cells. Therefore

counts made a day after injection would give a better measure of the presence of radioactive phosphorus incorporated into a mass of metabolically active cells. In their recent work Eisenberg⁹ et al., have confirmed the importance of the count made 24 hours following injection.

In our initial studies we made counts both at one and two hours, and again at 24 hours following injection. The one- and two-hour counts were of so little value that we soon abandoned them and relied only on the count made at 24 hours. In certain cases it is probable, however, that the differentiation of neoplastic lesions may be helped by studying the activity ratio at varying intervals following the intravenous administration of radioactive phosphorus. In this way a time curve of the relative activity could be obtained. In one group of normal eyes the time curve was established by making periodic counts up to eight days following the injection. At the end of 24 hours the count over the normal eye was found to be about one half that present at the end of the first hour. At the end of five days the count from an area in the normal eye had dropped to approximately one third of the count found at the end of the first hour following injection. Neoplasms tend to retain radioactive phosphorus longer than normal tissues. Therefore a comparison of the rate of drop over the tumor to that over the control reference area may prove useful.

The second controversial point is the selection of the site to be used for the normal reference count. Eisenberg⁸ et al. have used the mean of four counts made at the limbus of the fellow normal eye. With this method a count from one anatomic position in the abnormal eye may be compared, in certain cases, with the count from a different anatomic position in the fellow normal eye. Since counts vary in different anatomic positions, the site for the reference count should ideally be the area in the normal eye that corresponds to the position of the lesion in the abnormal eye.

In some cases the corresponding anatomic position in the normal eye cannot be used for the reference count. This is true in patients with bilateral lesions, such as bilateral retinoblastomas. In these cases some non-ocular reference point, such as the lip or ear lobe, may be used. However, for the interpretation of such results, many normal cases will have to be studied to establish the usual relationship of counts over the eye to those over the lip or ear lobe. In our series, counts were made over the lip in 19 patients and in them the counts in the normal eye ranged from one fourth to one half those from the lip. This information was helpful in studying a patient with bilateral retinoblastomas. In this patient the count over the lesion in the left eye was 99 percent of the count over the lip. The count over the right eye was 80 percent of the count over the lip, indicating a concentration of radioactivity in the retinoblastomas. It would be well for all clinics interested in the use of radioactive phosphorus to decide on the most suitable nonocular reference point. Then data could be collected to establish the relationship between the count over the normal eye and the standard nonocular reference point chosen.

The corresponding anatomic position in the normal eye cannot be used for the reference count in those cases with posterior lesions. When searching the posterior portions of the globe, an incision in the conjunctiva

and Tenon's capsule will be necessary. Obviously, it would be unwise to operate on the normal eye for the sole purpose of exposing the area corresponding to the lesion in the abnormal eye. In these cases two possible choices for the reference site can be made. One is the position in the normal eye, accessible without operation, that corresponds as closely as possible to the position of the lesion in the abnormal eye. The other choice is the site in the abnormal eye as far removed as possible from the site of the lesion. It has been the general experience in our patients with neoplasms that the counts drop off rapidly as the counter is moved a short distance away from the site of the tumor.

CONCLUSIONS

1. With the present technique the use of radioactive phosphorus is a helpful test for detecting the presence of intraocular tumors in the anterior segment. Present experience indicates that the method may also be useful in posterior lesions when counters become available for searching the posterior segment.

2. Further study is needed to determine the optimum time to make the count following the injection. Present evidence suggests that the counts should be made at least 24 hours after the injection of radioactive phosphorus.

3. The most satisfactory site for the reference count is the area in the normal eye corresponding to the location of the lesion in the abnormal eye. Since in a few cases it is not practical to use this ideal site, a nonocular area, such as the lip or ear lobe, should be standardized, so that data may be collected to determine the usual ratio between the count from the eye and the selected nonocular site.

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THE VIABILITY OF FRESH AND FROZEN CORNEAS*

AS DETERMINED IN TISSUE CULTURE

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The recent paper by Eastcott¹ and his associates on the preservation of corneal grafts by freezing has stimulated renewed interest in the problem of preserving corneas removed at death for later transplantation. Unsuccessful attempts have been made by many investigators to preserve corneas for long periods of time as donor material by formol fixation,² drying,³ freezing,⁴ and freeze-drying.^{5,6}

The good clinical results reported by Eastcott seem to be due to the use of glycerol in the method of preservation to protect the

cornea from the harmful effects of freezing and thawing. In 1949, Polge, Smith, and Parkes⁷ found that fowl spermatozoa protected with glycerol and saline retained their motility after freezing and thawing. Similar treatment has been used to preserve viability of other tissues, such as endocrine tissue, spermatozoa, skin, and red blood cells.⁸⁻¹⁰

It has long been assumed by most ophthalmologists that, in order to obtain a clear graft, one must use donor material which is viable. If this is true, it appears that Eastcott and his associates have produced a means of preserving and storing corneas which makes available viable donor material when needed. They reported the results of five lamellar and seven partial penetrating grafts performed in 12 patients. The donor

* From the Naval Hospital, the Tissue Bank of the Naval Medical School, the Naval Medical Research Institute of the National Naval Medical Center, and the Tissue Culture Section, Laboratory of Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

material consisted of human corneas removed within 12 hours of death which were soaked in 15-percent glycerol and quick frozen in carbon dioxide and alcohol slush. The corneas were stored at -79°C . for intervals of three days to nine months. All of the lamellar grafts remained clear and were considered to be successes. Of the partial penetrating grafts, two were considered to be successes with final clarity of the grafts, three were considered to be partial successes with partial clarity of the grafts, and two were failures with complete opacification of the graft. There seemed to be little correlation between the time of storage of the donor material and the final clarity of the graft.¹

Because of the good results obtained in the clinical use of corneas preserved in this manner, an attempt was made to determine whether or not animal corneas preserved in a similar manner were viable. Tissue culture was selected as the best means of determining the viability of both fresh and preserved corneas.

GENERAL MATERIALS AND METHODS

The animals used in these experiments were rabbits of an average body weight of approximately 3,000 gm. Each of the animals was killed at the Naval Medical Research Institute. Immediately after death both corneas were removed with keratome and scissors under sterile conditions. The corneas were excised within the limbus so that no conjunctival or scleral tissues were included. The corneas were then treated in one of the following ways:

A. *The corneas referred to as "fresh"* were placed in Pyrex test tubes containing stock tissue culture medium* and were transported to the Tissue Culture Laboratory at the National Cancer Institute within 30 minutes. There the corneas were divided into equal halves and each half was placed in a

Carrel D, 3.5 flask in plasma clot under OC perforated cellophane. The flasks were then incubated at 37.5°C . with horse serum tissue culture medium, as used in that laboratory, as the nutrient substance.

B. *The corneas referred to as "soaked"* were placed in test tubes which contained 15-percent glycerol U.S.P. by volume in either Earle's balanced buffered saline or in Ringer's solution and allowed to remain for one hour. The corneas were then transported to the Tissue Culture Laboratory where they were divided, explanted, and incubated as previously described.

C. *The corneas referred to as "frozen"* were frozen either with (1) no previous soaking, (2) after soaking in 15-percent glycerol in Earle's¹¹ balanced saline for one hour, or (3) after soaking in 15-percent glycerol in Ringer's solution for one hour. The excess fluid was decanted and the test tubes containing the corneas were immersed in a container of carbon dioxide-alcohol slush at -79°C . for three minutes. The test tubes were then capped and placed in a dry-ice chest at -79°C . At the end of one hour they were removed and the corneas were rapidly thawed by immersing the test tubes in a water bath at 38°C . for two minutes (fig. 1). The specimens were then transported within 30 minutes to the Tissue Culture Laboratory where they were divided into two equal halves, explanted, and incubated as previously described.

All specimens were examined microscopically, periodically for 48 hours, the results recorded, and the specimens then discarded.

RESULTS

The results of all experiments are shown in Table I and detailed in the text as follows:

Experiment 1. Ten corneas were treated as "fresh" control material. Ten were soaked in 15-percent glycerol in Earle's balanced saline. Ten were soaked in an identical solution for one hour and then frozen. Thus 30 corneas yielding 60 specimens were explanted.

* This stock tissue culture medium contained: Earle's¹² balanced saline 40 percent, horse serum 40 percent, extract from 10-day chick embryo (filtered) 20 percent.

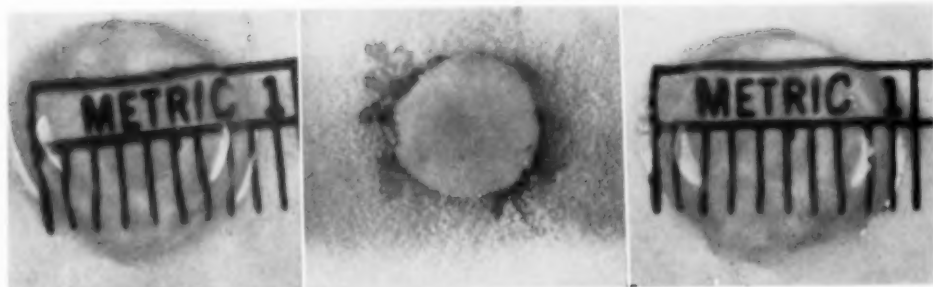


Fig. 1 (McPherson, et al.). Cornea: (A) Prior to freezing. (B) Frozen, after glycerol soaking. (C) After thawing.

Within a few hours evidence of viability could be seen in most of the "fresh" cultures, and within 48 hours in all cultures. The earliest signs of viability were a migration of marginal polygonal cells which resembled epithelium; this was accompanied by lysis of the plasma clot (fig. 2). This was followed by a secondary wave of migration of elongated spindle-shaped cells which resembled fibroblasts or corneal stromal cells (fig. 3). Although there was an initial lag period in onset of migration of living cells from the explants of frozen corneas, there seemed to be little difference in the appearance of the cultures of fresh, glycerol soaked, or frozen specimens in 48 hours. All showed an extensive area of cell migration grossly (fig. 4).

Experiment 2. This was undertaken to see if there was any apparent difference in the viability of glycerol protected frozen corneas and unprotected frozen corneas. Two corneas

were treated as "fresh" controls. Six corneas were soaked in 15-percent glycerol in Earle's balanced saline and then frozen. Six corneas from fellow eyes were frozen without prior soaking in glycerol. Twenty-eight cultures were obtained.

The four "fresh" control cultures showed rapid migration of live cells from the explant. The 12 cultures of six corneas soaked in glycerol and then frozen all showed migration of polygonal cells within 24 hours. This was followed by a migration wave of spindle cells within 48 hours. Of the 12 cultures of the six corneas frozen unprotected, migration occurred in only six cultures within 48 hours. In these seven the extent of migration was not as great as that which occurred in the preceding series; cell vacuolization was much more severe than in any preceding group.

Experiment 3. Because the previous experiment suggested that there was a differ-

TABLE 1
RESULTS OF EXPERIMENTS

	Number of Cultures	Fresh		Soaked Glycerol & Earle's Solution		Soaked Glycerol & Ringer's Solution		Frozen Unprotected		Frozen Glycerol & Earle's Solution		Frozen Glycerol & Ringer's Solution	
		+	-	+	-	+	-	+	-	+	-	+	-
Results:													
Experiment 1	60	20	0	20	0	+	-	+	-	20	0	+	-
Experiment 2	28	4	0					7	5	12	0		
Experiment 3	120	20	0	20	0	20	0	16	4	20	0	20	0
Total	208	44	0	40	0	20	0	23	9	52	0	20	0

+ Indicates migration of living cells.

- Indicates no migration.

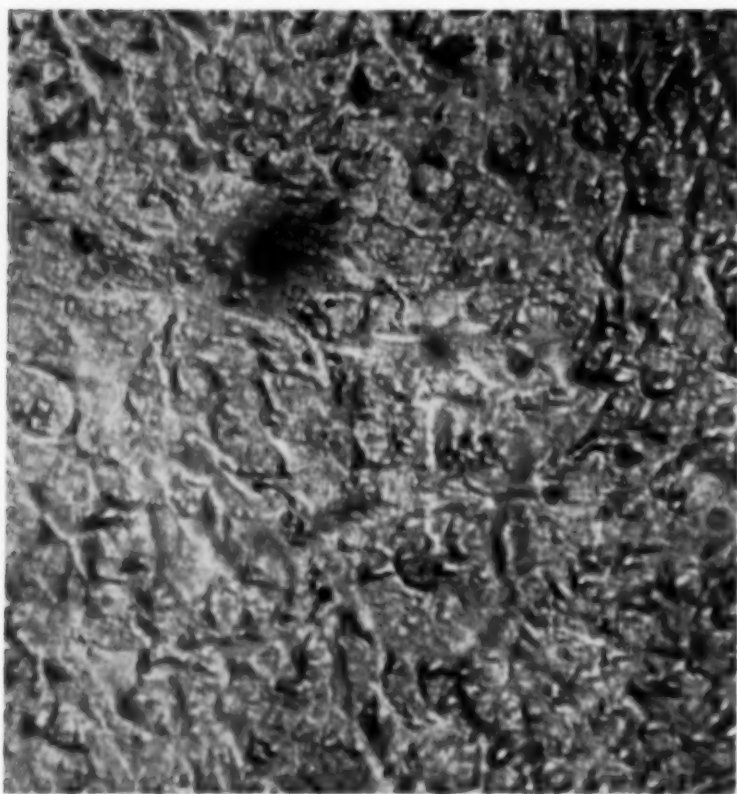


Fig. 2 (McPherson, et al.). Migration of epithelial-like cells from explant of a frozen cornea in tissue culture.

ence in the viability of frozen corneas, protected and unprotected by glycerol, a third experiment was undertaken using the following experimental conditions with 20 cultures in each: fresh corneas, corneas soaked in 15-percent glycerol in Earle's balanced saline, corneas soaked in 15-percent glycerol in Ringer's solution, frozen corneas unprotected by glycerol, corneas frozen after soaking in 15-percent glycerol in Earle's balanced saline, and corneas frozen after soaking in 15-percent glycerol in Ringer's solution.

Within 48 hours extensive migration of living cells occurred in cultures of all corneas except in those corneas frozen unprotected by glycerol. Of the 20 cultures of these unprotected frozen corneas, 16 showed only limited migration. In four there was no mi-

gration whatsoever. In the 16 which showed some migration, the migrating cells showed extensive vacuolization. The growth patterns were the same as in previous experiments with an early stage of migration of epithelial-like cells followed by the migration of spindle cells resembling corneal stromal cells.

COMMENT

Before beginning the present study the feasibility of using human corneas was considered. However, because of the difficulty of obtaining a sufficient quantity under constant conditions and at constant times after death, it was decided to use animal corneas. Rabbits were selected as the animal of choice since most of the experimental work to date has been performed using them.^{8,9,12,13}

Three possible tests of viability were considered. These were clarity of the donor cornea after transplantation, tests of the respiratory enzyme systems, and the tissue culture test of cell migration. Actual transplantation of the donor material was discarded as a test since this is based on the assumption that a clear graft must indicate a viable donor cornea, an assumption that had not been proven. Testing of the enzyme systems was discarded since enzyme systems may continue to function in corneas in which there are no living cells and which are no longer suitable donor materials.¹⁴ Tissue culture was selected as the method of choice since it offers a critical test of viability.

Human and animal corneas have previously been cultured in tissue culture. Filatov and Bajenova¹⁵ reported the successful cultivation of both fresh and partially dehydrated rabbit corneas in Carrel dishes. Hoffman and Messier¹⁶ reported the cultivation of rabbit corneas in tissue culture using fresh material. They were unable to cultivate rabbit

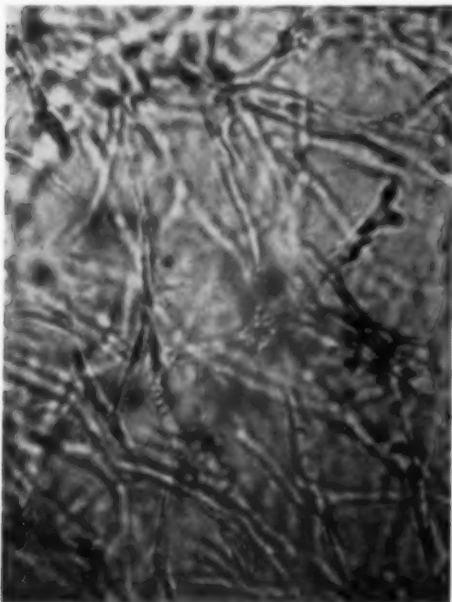


Fig. 3 (McPherson, et al.). Migration of spindle cells resembling corneal stromal cells from an explant of a frozen cornea in tissue culture.

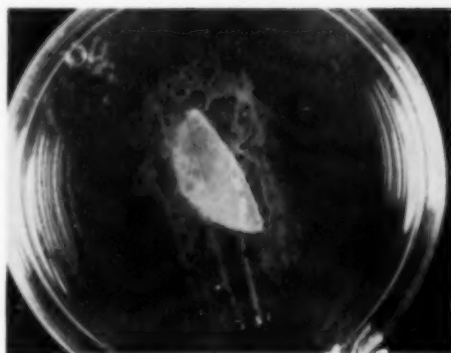


Fig. 4 (McPherson, et al.). Explant of a frozen cornea in tissue culture, showing a surrounding epithelial sheet.

corneas which had been frozen and stored.¹⁷ More recently Fowle and Ormsby reported the successful cultivation of fresh human and monkey corneas using Carrel D, 3.5 flasks and a plasma clot.¹⁸ They found that the migration of monkey corneal epithelium was apparent after 24 hours in most cultures; the success of growth seemed to depend in part on having an explant of large size. Fibroblastic migration was seldom observed in less than three to four days and frequently did not appear for 10 days. No mention was made of the growth of endothelium.

In the present study we were able to observe the migration of epithelial-like cells within 24 hours in all fresh or glycerol protected frozen corneas, while both epithelial-like and fibroblastlike cells appeared within 48 hours. Whether this difference between the migration rate of the cells as observed by Fowle and Ormsby, and in our own study was due to the difference in animals used or to a difference in tissue culture technique is not apparent. In any event, migration within 48 hours was a constantly reproducible finding in our experiments. In no instance were we able accurately to identify migration of endothelial cells. This is in accord with the experience of previous investigators. This may be because of the difficulty of cell identification in tissue cul-

ture and the resemblance of endothelium to epithelium, or because the endothelial cells are simply outnumbered by other cells in the cornea.

Prior to the present study, the viability in tissue culture or grafts of rapidly frozen tissues has been demonstrated only with skin and thyroid.¹⁹ The success of the present study in demonstrating such viability seems to be associated with three factors: (1) glycerol soaking, (2) fast freezing, and (3) fast thawing. The failure of fast freezing alone to preserve rabbit corneas has been previously noted by Smelser and Ozanics.⁴ These investigators were unable to produce clear grafts using donor material which had been frozen to -195°C . in liquid nitrogen. They did not protect donor material by prior soaking in glycerol, and thawing was accomplished by allowing the material to stand at room temperature. In the present study corneas frozen without prior soaking did show limited viability with migration occurring in 23 of 32 cultures. This continued viability may have been due to the relatively short duration of storage after freezing or to the technique of fast thawing; since Billingham⁹ has shown that slow thawing results in a lower incidence of viability.

Smith¹⁹ and Lovelock²⁰ consider that the harmful effects of freezing are caused by the formation of ice crystals with actual mechanical damage to the cells, and by a lethal increase of salt concentration in the medium in which the cell is suspended. They found that this lethal concentration seems to occur at some point between 0° and -40°C . Lovelock²⁰ has suggested that within this temperature range concentration of salts in solution may occur due to ice crystal formation, and that this more concentrated solution has some effect on the integrity of the cell through its action on certain lipids and lipoproteins of the cell membrane. He considers that the

hygroscopic properties of glycerol prevent the formation of intracellular ice crystals by partially withdrawing water prior to freezing²¹ and in addition glycerol seems to have some "buffering action" in protecting the cell from the sudden increase in electrolyte concentration.²⁰

Whatever the mechanism of action of the glycerol may be, in the present studies it has been possible to demonstrate routinely viability in tissue culture of those corneas which were soaked in glycerol prior to freezing. The viability of these corneas appeared greater than that found in those corneas frozen without previous soaking in glycerol.

SUMMARY

1. With tissue culture as a test of viability of both fresh and preserved corneas, the results of 208 cultures of rabbit corneas are described.

2. Cultures were grown in Carrel D, 3.5 flasks with a half cornea planted in each flask in a thin plasma clot under perforated cellophane covered by a nutrient fluid medium of horse serum and chick embryo extract in Earle's saline.

3. Fresh corneas showed excellent migration of epithelial and fibroblastic cells in all instances within 48 hours.

4. Corneas which were soaked in dilute glycerol or soaked and then frozen showed a slight lag in migration but were soon indistinguishable in migration and cell appearance from fresh corneas.

5. Corneas frozen without glycerol protection showed no migration in 28 percent of the cultures; the remainder showed retarded migration and severe cell injury.

6. The mechanism of glycerol protection from the harmful effects of freezing is discussed.

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ORBITAL RECONSTRUCTION*

UTILIZING TEMPORALIS MUSCLE

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The cosmetic deformity produced by exenteration of the orbit is extreme, and is the most distressing sequelae of the operation. Most of the modifications introduced in the operative technique have been concerned with methods of overcoming this deformity. These techniques may be grouped into several categories; first, operations¹ in which the

lids are preserved, and various techniques used to introduce an artificial eye into the socket; second, operations² in which the exposed orbital cavity is closed over anteriorly with skin; third, operations³ in which no attempt is made to correct the deformity surgically, but instead the deformity is merely masked by various prosthetic devices; and fourth, operations⁴ in which attempts are made to fill in the orbital cavity with various types of tissue.

I have attempted to solve this problem by

* From the Wilmer Ophthalmological Institute of The Johns Hopkins Hospital and University. Presented at the Wilmer Residents meeting April 1, 1954.

utilizing a portion of the temporalis muscle to replace the orbital contents. In cases in which the anatomic location and histologic character of the malignant orbital tumor allow preservation of the lids,⁸ this procedure should permit the patient to wear an artificial eye in a mucous-membrane lined socket and covered with normal lid tissue. In cases in which the lids are removed, this procedure should permit filling of all or part of the orbital cavity and still allow the covering of the socket with a prosthesis or with skin.

OPERATIVE TECHNIQUE

A curved skin incision about seven to eight cm. in length is made, concave forward within the hairline and about five cm. behind the superior temporal orbital margin. The temporal fascia covering the temporalis muscle is exposed. The temporal fascia is dissected from the anterior one third of the broad origin of the temporalis muscle, exposing the muscle. A pedicle of temporalis muscle attached below is created by removing the anterior one-third of the muscle from its origin in the temporal fossa. The entire outer aspect of the lateral orbital wall is then exposed.

A large window is cut out of the lateral orbital wall using a Stryker saw. The window is made as far posteriorly as possible. The orbital margin is left intact. The muscle pedicle is then stuffed through the window into the previously exenterated orbit. Temporal fascia is replaced and the skin incision closed. No drain is necessary. Bleeding is controlled by local infiltration of procaine or Xylocaine containing epinephrine and hyaluronidase.

CASE REPORT

History. E. B., a 19-year-old white youth was first seen on January 27, 1954, because of a foul-smelling right orbit. Seventeen years previously the right eye had been enucleated because of panophthalmitis following a perforating injury. During the following

14 years the patient wore an artificial eye. Three years previously, the prosthesis began to protrude, and on March 29, 1951, an exenteration of the right orbit was carried out elsewhere. This included all the orbital contents including the periosteum of the orbit, but did not include the lids. The orbit was lined with a split-thickness skin graft taken from the chest and abdomen. No tumor was found on histologic examination of the tissue removed. Two months later a plastic procedure was done on the lateral canthus. Postoperatively the right orbit remained dark in color and foul smelling, with considerable foul discharge. The patient was unable to wear any prosthesis.

Examination here showed the left eye to be entirely normal. The lids on the right were closed over an exenterated orbit. There was good orbicularis action. The entire inner aspect of the orbit was covered with a foul-smelling, golden-brown and black moist tissue. X-ray studies showed no evidence of osteomyelitis. Culture showed *B. pyocyaneus*. The patient was admitted to the Wilmer Institute, the orbit was cleaned mechanically, and the infection cleared with local and systemic chemotherapy. On February 4, under pentothal anesthesia, the skin lining the orbit was tediously removed and temporalis muscle was placed in the orbit, as described.

Postoperatively, the patient experienced transient difficulty in opening his jaw widely. This responded well to time and chewing exercises. The temporalis muscle thrived in the orbit and adequately filled the cavity. Two months later peritoneum was transplanted to the posterior aspect of both lids and to the muscle tissue in the orbit. This healed uneventfully, giving an adequate mucous-membrane lined cavity. However, 18 months later, there had been some contraction of the socket, and it will be necessary to enlarge this in the future. A residual depression in the anterior portion of the temporal fossa persists.

COMMENT

So far this procedure has been used in only one case. The excellent result in this case, as well as the relative infrequency of orbital exenteration, prompt this report.

Temporalis muscle may be utilized to fill the orbit either immediately upon completion of exenteration or, as in the case reported, sometime after exenteration. Various methods of covering the orbit anteriorly may be carried out, depending upon the particular circumstances in each case. If the lids have been removed, it would seem best to cover the temporalis muscle with skin, either as a sliding flap or as a split-thickness Thiersch graft. If the lids have not been removed, then the temporalis muscle may be covered

with mucous membrane from any of the available sources, according to the technique and preference of the particular surgeon.

It would seem that this technique might be carried out in most cases that require orbital exenteration or orbito-sinus exenterations. However, in cases in which postoperative irradiation might be effective, it is probably contraindicated, at least as an initial procedure.

SUMMARY

A new technique of orbital reconstruction utilizing temporalis muscle has been described, and the result in a single case is reported.

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THE EFFECTS OF ACETAZOLEAMIDE ON ASCORBIC-ACID TURNOVER*

AN APPLICATION OF THE THEORY OF AQUEOUS HUMOR DYNAMICS

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I. INTRODUCTION

Ascorbic acid has provided a convenient test substance for studying the rate of flow of aqueous and for applying the methods of analysis described in the preceding paper.¹ The presence of ascorbate in high concentration in intraocular fluids and its ease of determination has led to its repeated use in measuring turnover rate in the anterior chamber.²⁻⁴ More recently, the posterior chamber aqueous has been demonstrated to contain a higher concentration of ascorbate than the anterior chamber.⁵ This difference has been adequately explained on the basis of diffusional losses from the anterior chamber.⁶

Following parenteral administration of sodium ascorbate to rabbits, the concentration in the aqueous humor was found to rise to saturation level.⁷ The determination of the rates of these rises in both the posterior and anterior chamber fluids was the purpose of these experiments. Application of the exponential and linear (X, Y) methods of analysis to these data has provided independent values for aqueous flow as well as other coefficients relative to the dynamics of ascorbate in the rabbit eye. Furthermore, the availability of carbonic anhydrase inhibitors that are capable of partially suppressing aqueous humor formation^{8,9} permitted experimental alteration of these coefficients.

Ascorbic-acid turnover data in rabbits subjected to acetazoleamide offered additional

opportunities for exponential and linear analyses. Moreover, the flow constants obtained from such analyses provided independent measures of the degree of inhibition of aqueous secretion induced by acetazoleamide.

II. METHODS

Male, albino rabbits, weighing two to three kg. (Haskins Rabbitry, Saint Louis), were used throughout this study. Nephrectomized rabbits had both kidneys removed through a posterior incision 18 to 24 hours before tapping the eyes.

Blood which was obtained by cardiac puncture with a heparinized syringe was centrifuged at once in the cold. Posterior and anterior chamber fluids were withdrawn from the tetracaine anesthetized, proptosed eye into a calibrated pipet. In order to avoid metallic oxidation of ascorbate, it was found necessary to use a 26-gauge platinum needle embedded in the pipet. Pipets were used repeatedly, but cleaned and dried between uses by drawing hot dilute Sterox, distilled water, and absolute alcohol through them.

Samples were introduced at once into four-percent metaphosphoric acid and titrated immediately with dichlorophenolindophenol, using a 0.1 ml. Gilmont ultramicroburet. All anterior chambers and plasmas were run in triplicate, but posterior chambers were usually determined as single samples.

Acetazoleamide (Diamox[†]) was administered as an isotonic solution of the sodium salt in a single dose of 100 mg./kg. shortly after nephrectomy. Sodium ascorbate was injected in doses of 50 mg./kg. intravenously

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[†] Diamox used in this study was furnished through the courtesy of Dr. James Gallagher of the Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

TABLE 1
 ASCORBIC-ACID TURNOVER IN THE EYES OF NONTREATED RABBITS^b

Time (min.)	No. Eyes	C _p	C _a	C _b	$\frac{dC_a}{dt}$
0	10	23.5	18.0	—	—
5	5	38.5	19.9	31	0.38
10	5	46.5	21.5	22	0.40
20	5	57.0	26.4	15	0.48
40	5	60.0	34.0	15	0.36
60	5	62.5	39.6	15	0.26
90	5	64.0	45.5	15	0.17
120	5	65.5	49.2	15	0.11
180	5	68.0	54.5	15	0.06
240	5	69.5	57.1	15	0.04
300	6	71.0	58.9	15	0.03
360	5	72.0	61.0	15	0.02
18-24 hrs.	22	75.0	65.0	20	0.0

^b = intact and nephrectomized.C_p = average posterior chamber concentration ascorbic acid (mg. %).C_a = average anterior chamber concentration ascorbic acid (mg. %).C_b = average plasma concentration ascorbic acid (mg. %). $\frac{dC_a}{dt}$ = rate of change of anterior chamber concentration ascorbic acid (mg. % per minute).

dt

followed in 15 minutes by 20 mg./kg. subcutaneously and then 20 mg./kg. subcutaneously every 40 minutes to intact rabbits and every 60 minutes to nephrectomized rabbits. This dose schedule was found empirically to result in an almost constant average plasma ascorbate level of 15 mg. percent for the time interval of 20 minutes to 360 minutes. The

plasma levels at five and 10 minutes after the intravenous injection averaged 31 mg. percent and 22 mg. percent respectively. For 18 to 24 hour data, nephrectomized rabbits were injected subcutaneously with 200 mg./kg. of sodium ascorbate shortly after nephrectomy. This resulted in average plasma ascorbate levels of 20 mg. percent.

 TABLE 2
 ASCORBIC-ACID TURNOVER IN THE EYES OF ACETAZOLEAMIDE^b-TREATED RABBITS^d

Time (min.)	No. Eyes	C _p	C _a	C _b	$\frac{dC_a}{dt}$
0	10	31.1	19.0	—	—
5	5	46.4	20.3	31	0.27
10	5	59.8	21.7	22	0.32
20	5	73.9	25.3	15	0.37
40	5	86.0	32.9	15	0.37
60	5	91.0	40.2	15	0.32
120	5	97.5	54.0	15	0.20
180	5	102.0	63.0	15	0.13
240	5	105.5	69.5	15	0.08
300	6	108.0	74.0	15	0.06
18-24 hrs.	16	115.0	85.0	20	0.00

^b = 100 mg./kg. of sodium salt of Diamox at times of nephrectomy.^d = all rabbits nephrectomized.C_p = average posterior chamber concentration ascorbic acid (mg. %).C_a = average anterior chamber concentration ascorbic acid (mg. %).C_b = average plasma concentration ascorbic acid (mg. %). $\frac{dC_a}{dt}$ = rate of change of anterior chamber concentration ascorbic acid.

dt

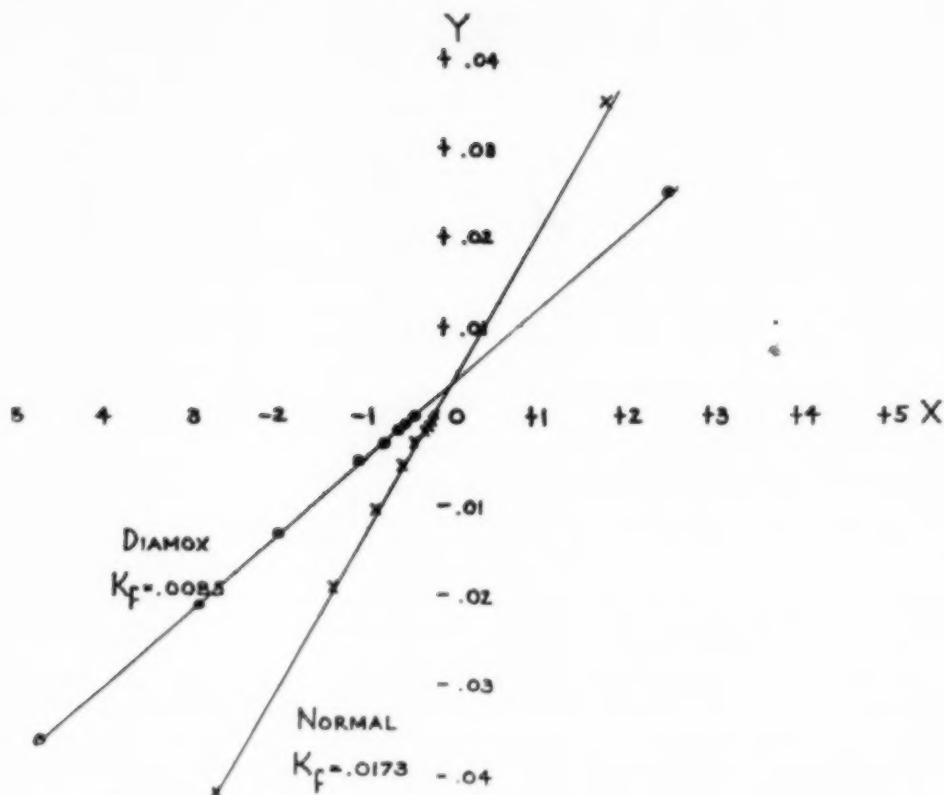


Fig. 1 (Becker). Linear (X-Y) analysis of ascorbic acid turnover in acetazolamide treated (-o-o-o-) and untreated (-x-x-x-) rabbits. The slopes of the straight lines obtained provide values for K_f , the flow coefficients. The diffusion factors, K_d , are determined by the Y-intercepts of the plots.

In each animal samples of aqueous humor were withdrawn from each eye at different time intervals after injecting ascorbate. Each eye was used only once and animals were then discarded. The normal ascorbate series consisted of 88 eyes of 44 rabbits (25 of these rabbits were nephrectomized animals). The acetazolamide series consisted of 72 eyes of 36 nephrectomized rabbits.

III. RESULTS

In the nontreated series, no significant differences were noted between nephrectomized and intact rabbits at any of the time intervals. All values were, therefore, averaged for various time intervals after ascor-

bate injections and are presented in Table 1 for rabbits not subjected to carbonic anhydrase inhibition. In Table 2 are shown the data at similar time intervals in the acetazolamide-treated series.

A. LINEAR ANALYSIS

By plotting the concentration of ascorbate in the anterior chamber (C_a) against time in minutes (t), values were obtained for the rate of change of anterior chamber concentration of ascorbate, dC_a/dt from the slope of the plot at each time interval. Values for dC_a/dt each time are presented in Tables 1 and 2.

In the equation:¹ $Y = K_f X + K_d$ where

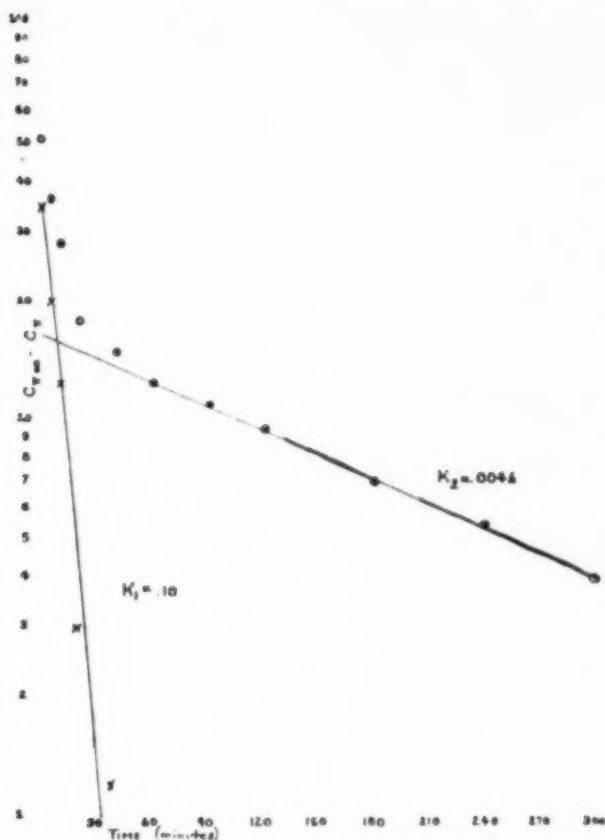


Fig. 2 (Becker). Graphic exponential analysis of data on posterior chamber concentrations (C_p) of ascorbate at various times (t) following parenteral administration in untreated rabbits. The ordinate plotted ($-o-o-o-$) is the $\log (C_p - C_\infty)$ where C_∞ is the steady-state value (75 mg. percent). A straight line with slope $K_2 = 0.0046$ is fitted to the linear tail of the curve. The points ($-x-x-x-$) are obtained by subtracting the K_2 line from the original posterior chamber curve. The straight line best fitting these points has a slope $K_1 = 0.10$.

$$Y = \frac{dC_p}{(C_p - C_\infty)dt}$$

$$X = \frac{C_p - C_\infty}{C_p - C_\infty}$$

K_1 = rate of flow of aqueous per minute as a fraction of the volume of the anterior chamber

K_2 = rate of diffusional exchange of ascorbate between anterior chamber and plasma

C_p = plasma ascorbate concentration

C_∞ = posterior chamber ascorbate concentration

the values of X and Y are available from the experimental data of Tables 1 and 2. In the plot of X versus Y , the slope of the line obtained provides a value for the flow coefficient (K_1) and the Y -intercept supplies the diffusion constant (K_2) for ascorbate. In Figure 1 the data are plotted both for the normal ($-x-x-x-$) and acetazolamide-treated

($-o-o-o-$) rabbits. It is apparent that both the normal and acetazolamide data may be fit readily with straight lines as predicted by the theory presented.¹ Furthermore, the plots for these two groups of animals are quite discrete from one another. Diffusion and flow coefficients can be readily determined for both groups of animals. The normal diffusion coefficient of 0.0045 per minute for ascorbate remains essentially the same (0.0040) after acetazolamide is administered. However, the value for flow of 0.0173 per minute in the untreated rabbit is reduced to 0.0085 per minute following carbonic anhydrase inhibition (51 percent inhibition of flow).

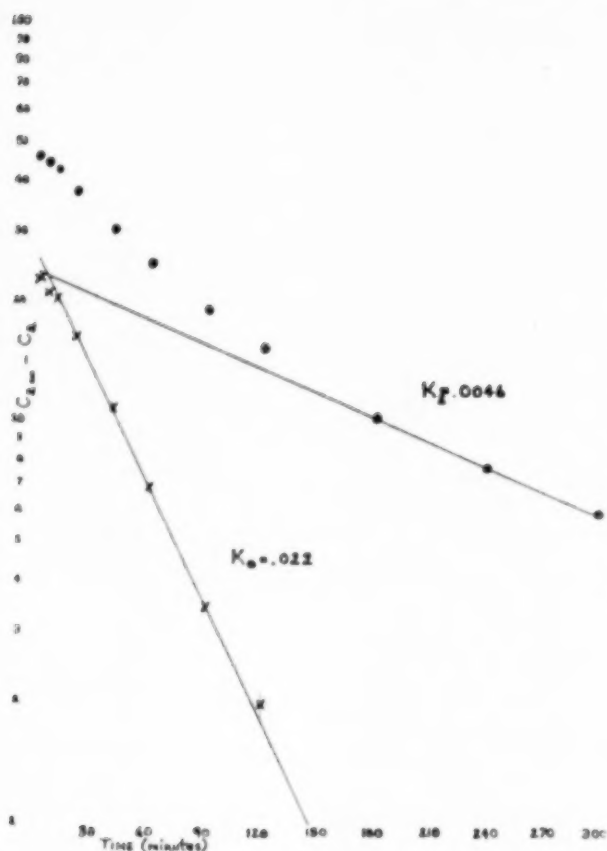


Fig 3 (Becker). Graphic exponential analysis of data on anterior chamber concentrations (C_a) of ascorbate at various times (t) following parenteral administration in untreated rabbits. The ordinate plotted ($-o-o-o-$) is the $\log (C_{as} - C_a)$ where C_{as} is the steady state value (65 mg. percent). A straight line with slope of the tail ($K_t = 0.0046$) is obtained from the posterior chamber data of Figure 2. Subtracting this line from the original anterior chamber data results in points ($-x-x-x-$) which form a straight line with slope $K_a (= K_t + K_d) = 0.022$.

B. EXPONENTIAL ANALYSIS

The graphic exponential analysis of the normal posterior chamber data is presented in Figure 2. Here are plotted ($-o-o-o-$) $\log (C_{ps} - C_p)$ versus time (t) where C_{ps} is the steady state concentration of ascorbate in the posterior chamber and C_p is the concentration at time (t). An excellent linear tail is obtained with a value for the slope of 0.0046 which provides us with the reservoir filling coefficient (K_2). Subtracting this line from the original data yields another straight line ($-x-x-x-$) of slope 0.10, the turnover rate of ascorbate in the posterior chamber (K_1). It is apparent that a double exponential fits the posterior chamber ascor-

bate data remarkably well.

In Figure 3 are plotted ($-o-o-o-$) $\log (C_{as} - C_a)$ versus time, where C_{as} is the steady state concentration of ascorbate in the anterior chamber and C_a is the concentration at time, t . Subtracting the linear tail of the same slope ($K_t = 0.0046$) obtained from the posterior chamber graph, from the plot of $\log (C_{as} - C_a)$ versus time results in a line ($-x-x-x-$) with slope of 0.022. This is the value for K_a , the turnover rate as ascorbate in the anterior chamber and is equal to the sum of the rates of diffusional exchange and flow for the anterior chamber ($K_a = K_d + K_t$). From the steady state data at 18 to 24 hours for normal rabbits, one can estimate

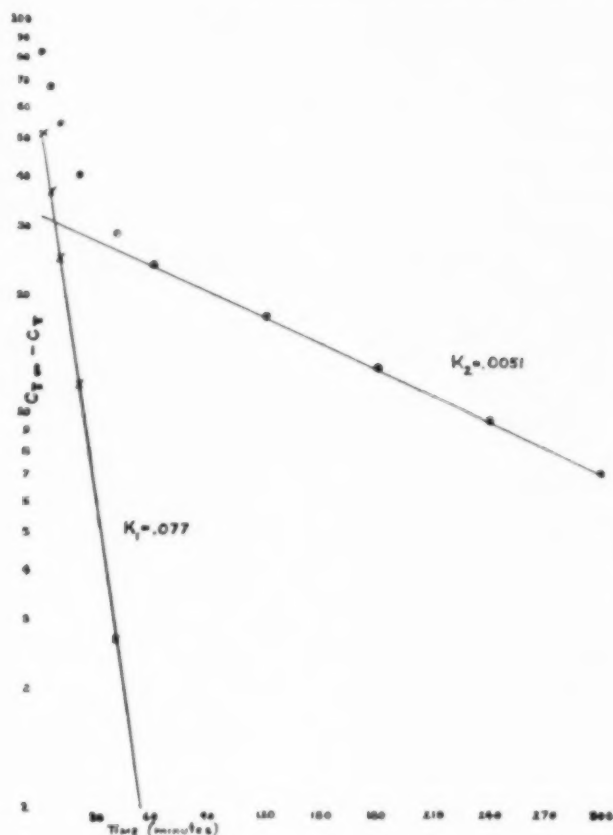


Fig. 4 (Becker). Graphic exponential analysis of data on posterior chamber concentrations (C_p) of ascorbate at various times (t) following parenteral administration in acetazoleamide treated rabbits. The ordinate plotted ($\circ-\circ-\circ$) is the $\log (C_p - C_{\infty})$ where C_{∞} is the steady-state value (115 mg. percent). A straight line with slope $K_2 = 0.0051$ is fitted to the linear tail of the curve. The values ($\times-\times-\times$) are obtained by subtracting the K_2 line from the original posterior chamber curve. The best straight line that fits these points has a slope $K_1 = 0.077$.

the value for the ratio,

$$\frac{K_f}{K_d} = \frac{C_{as} - C_{ps}}{C_{ps} - C_{ss}} = \frac{65 - 20}{75 - 65} = 4.5$$

or, $K_f = 4.5 K_d$

Combining this information with the value of 0.022 for $(K_f + K_d)$ results in values for the diffusion coefficient, K_d , of 0.004 and the rate of flow, K_f , of 0.018 for the rabbit eye not subjected to carbonic anhydrase inhibitors.

Precisely the same methods have been applied to the data obtained for the acetazoleamide-treated rabbits and are presented in Figures 4 and 5. Here again, a double exponential satisfies the posterior chamber data, as predicted by the theory, and similar

graphic analysis can be applied to the anterior chamber data. Value for $K_2 = 0.0051$; $K_d = 0.004$; $K_f = 0.009$; $K_1 = 0.077$ are evident from the plots.

IV. DISCUSSION

The application of the theory of aqueous humor dynamics to the ascorbic acid turnover data in rabbit eyes has proved most rewarding. The data presented for the non-treated animals yield a linear relation when plotted as X versus Y. The anterior chamber data may be readily analyzed exponentially. Both methods of analysis result in values for the diffusion (K_d) and flow constants (K_f) which are in excellent agreement with each other (table 3). Furthermore, the

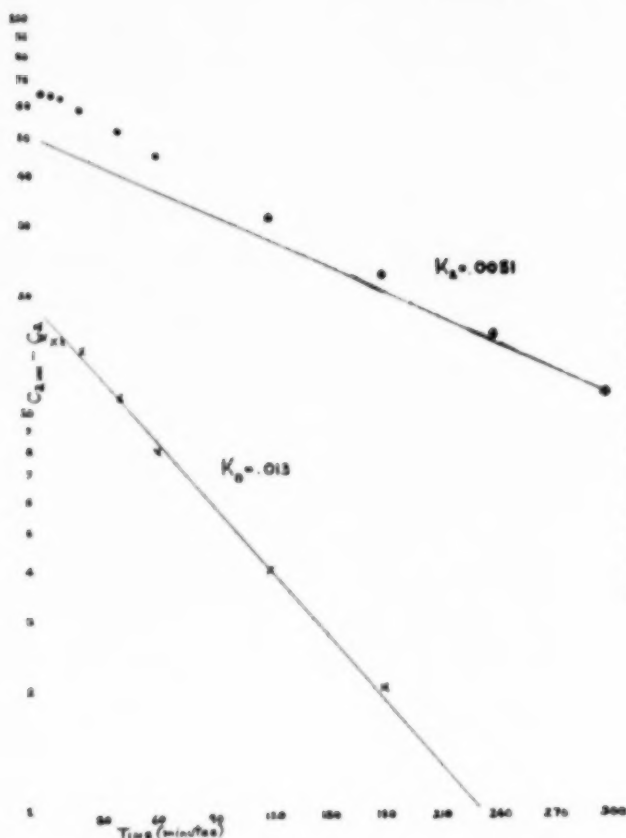


Fig. 5 (Becker). Graphic exponential analysis of data on anterior chamber concentrations (C_a) of ascorbate at various times (t) following parenteral administration in acetazolesamide treated rabbits. The ordinate plotted ($-o-o-o-$) is the $\log C_{a0} - C_a$ where C_{a0} is the steady-state value (85 mg. percent). A straight line with the slope of the tail ($K_2 = 0.0051$) is obtained from the posterior chamber data of Figure 4. Subtracting this line from the original anterior chamber data results in points ($-x-x-x-$) which form a straight line with slope $K_0 (= K_f + K_d) = 0.013$.

values obtained for normal flow (1.7 to 1.8 percent per minute) agree well with those reported for sodium (1.7 percent) and thiocyanate (2.0 percent) by Kinsey and Palm¹⁰ and are slightly higher than those obtained by Friedenwald¹ from the same sodium (1.4 percent) and thiocyanate (1.7 percent) data.

TABLE 3
COMPARISON OF LINEAR AND EXPONENTIAL
ANALYSIS OF ASCORBIC-ACID TURNOVER
DATA IN RABBITS

	Nontreated		Acetazolesamide	
	K_d	K_f	K_d	K_f
Linear	0.0045	0.0173	0.0040	0.0085
Exponential	0.004	0.018	0.004	0.009

It is also clear that rabbits subjected to carbonic anhydrase inhibition provide data which satisfy linear and exponential analyses and also yield results for K_d and K_f that agree for both methods (table 3). Moreover, the assumed lack of change in K_d following acetazolesamide¹² is confirmed. Even more exciting is the comparison of the alterations of aqueous flow induced by Diamox as determined by these direct methods of measurement and the estimates obtained previously by tonography¹¹ and changes in chemical composition of the aqueous¹² (table 4). In comparing these data, it must be recalled that in using ascorbate as a test substance, one is dealing with ascorbate "saturated" rabbits

TABLE 4
AVERAGE ALTERATION OF AQUEOUS FLOW
INDUCED BY ACETAZOLEAMIDE IN RABBIT
EYES

Method	% Change Flow
Tonography ¹¹	-63%
Steady state ¹²	
Bicarbonate	-64%
Ascorbic acid	-60%
Saturated ascorbic acid	-51%
Ascorbic acid dynamics	
XY analysis	-51%
Exponential analysis	-50%

and that this may increase the absolute rate of secretion by as much as 30 percent,⁸ as well as partially reverse the effects of acetazoleamide.¹³

V. SUMMARY

1. Linear analysis and graphic exponential analysis have been applied to ascorbic-acid concentrations found in the anterior and posterior chamber fluid of the rabbit eye at various times following parenteral ascorbate administration.

2. Rate of flow of aqueous humor is estimated at 1.7 to 1.8 percent per minute of the volume of the anterior chamber by both methods in the *ascorbate-saturated rabbit*.

3. Aqueous flow is reduced to 0.8 to 0.9 percent per minute in such rabbits by acetazoleamide administration (50 to 51 percent suppression of secretion).

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POSTERIOR LAMELLAR KERATOPLASTY*

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The purpose of this report is to describe a technique for posterior lamellar keratoplasty and to present a case of advanced Fuchs' endothelial dystrophy with aphakia in which this technique was utilized.

Stocker¹ and Paton² have reported successful visual results in Fuchs' dystrophy with penetrating keratoplasty. This technique is particularly applicable where the disease is localized to the central portion of the cornea. Where the condition is advanced, penetrating keratoplasty gives almost uniformly poor results.³⁻⁶ Franceschetti has advocated the "mushroom" graft in cases of Fuchs' corneal degeneration.⁷ Scraping of the corneal endothelium has been described by Paufigue and by Stocker.⁸

In advanced Fuchs' dystrophy removal of all or most of the diseased cornea by means of penetrating keratoplasty will usually require a 10-mm. keratoplasty or larger. Since many of these eyes are aphakic, such a procedure is especially hazardous. The technique to be described is carried out through a cataract-type incision. It therefore combines the safety of a cataract incision with the advantage of almost total removal of the diseased cornea.

TECHNIQUE

The donor eye is prepared in the usual manner for lamellar keratoplasty. The 10-mm. trephine is applied and a groove is cut approximately half way through the thickness of the cornea. Fixation sutures are applied and the anterior half of the cornea is dissected free with the Gill corneal knife. The anterior cornea is then discarded and the remaining posterior cornea of the donor eye is excised using the Katzin corneal scissors.

Attention is now directed to the recipient eye. A 10-mm. trephine is applied lightly to the cornea; the trephine is applied in a slightly eccentric position, such that its superior margin adjoins the limbus at the 12-o'clock position. Fluorescein is used to outline the trephine mark. A corneal groove is now made with the Bard-Parker knife along the trephine mark superiorly extending from the 9- to 3-o'clock positions (fig. 1-A). With the aid of a fixation suture the anterior half of the cornea is now undermined using the Gill corneal knife (fig. 1-B). The superior portion of the cornea can be readily undermined as in the usual type of lamellar keratoplasty. The inferior portion of the cornea is undermined with more difficulty; but this is made easier by inverting the Gill knife so that it follows the curve of the inferior cornea. Separation of the anterior and posterior halves of the cornea is extended to the limbus in all directions.

Up to this point the anterior chamber has not been entered. Excision of the posterior cornea is carried out by making a scratch incision into the anterior chamber along the site of the corneal groove. The Katzin corneal scissors are used to extend the incision. Fluorescein is reapplied to outline the original trephine mark; the fluorescein mark now serves as a guide for excising the inferior half of the cornea (fig. 1-C). Both the right-handed and left-handed Katzin scissors are used to carry the incision to the 6-o'clock position; the posterior half of the cornea is then removed from the anterior chamber.

Attention is now directed to the donor graft. Three double-armed sutures of 6-0 silk are passed into the graft at the 4-, 6-, and 8-o'clock positions, respectively (fig. 1-D). The sutures do not penetrate the full thickness of the graft and are placed so that they run parallel to the graft margin. Next, the 6-o'clock suture is passed into the an-

* Presented in part at the 14th Clinical Meeting, Wilmer Residents Association, Wilmer Ophthalmological Institute, March 31, 1955.

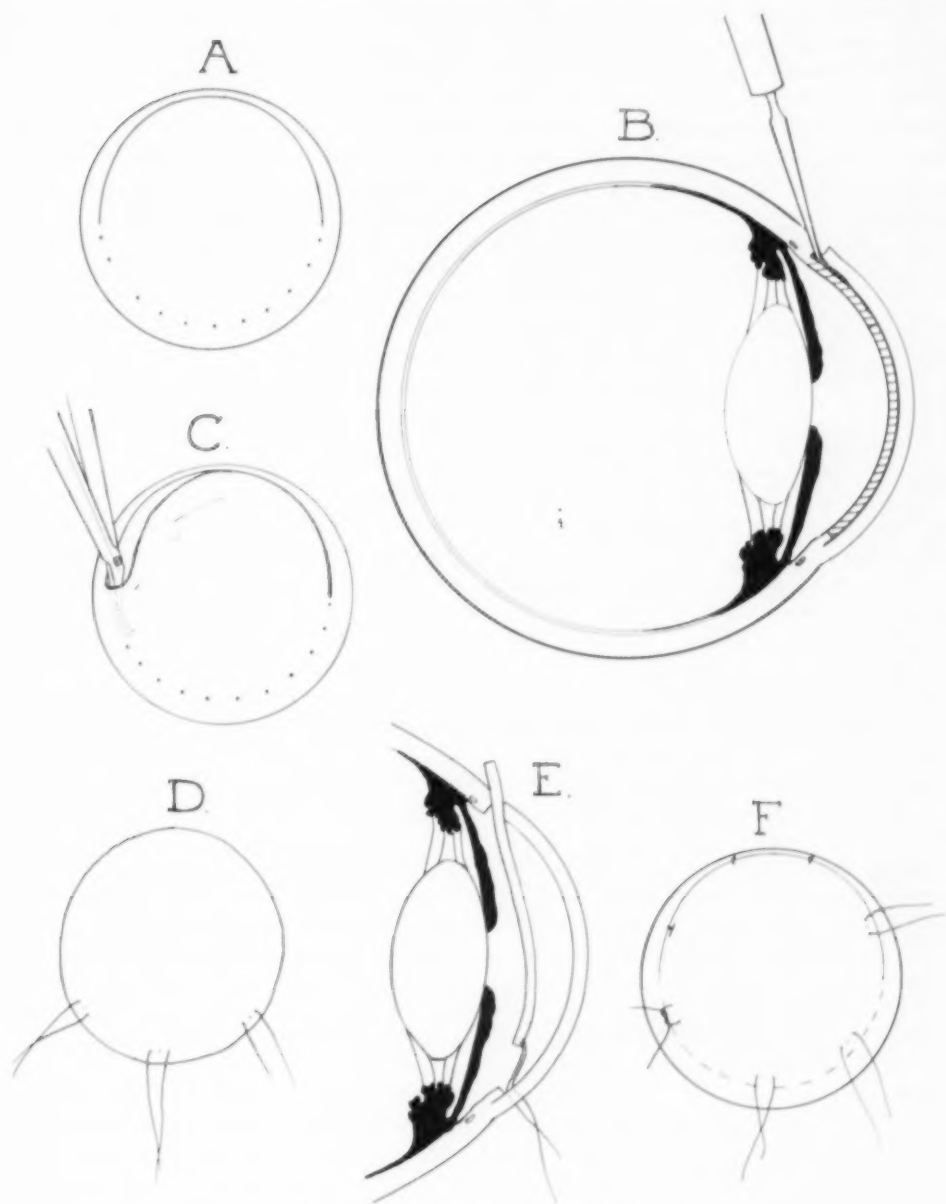


Fig. 1 (Tillett). Technique of posterior lamellar keratoplasty.

terior chamber with the needle holder and is passed through the recipient cornea at the 6-o'clock position (fig. 1-E). The graft is temporarily drawn into the anterior chamber and the exact point where the 4-o'clock suture touches the recipient cornea is marked by the assistant. The graft is now withdrawn and both arms of the 4-o'clock suture are passed through the recipient cornea at the place marked. The graft is again drawn into the anterior chamber, the position of the 8-o'clock suture is marked on the recipient cornea, and the graft is withdrawn. The 8-o'clock suture is passed through the recipient cornea. Following this the graft is once again drawn into the anterior chamber and all three of the sutures are pulled tight and tied. Additional sutures are placed at the 10- and 2-o'clock positions, securing the graft to the anterior cornea.

The corneal incision is now closed with postplaced sutures at the 11- and 1-o'clock positions (fig. 1-F).

CASE REPORT

The patient, J. J., a retired white man, aged 68 years, had been followed intermittently at the Wilmer Institute for many years because of congenital cataracts. In the past he had been able to read and get around without difficulty. In 1931, at the age of 45 years, he noted increasing failure of vision due to increasing cataract formation, and in 1947 at the age of 61 years he was forced to give up working. By 1951, his vision had dropped to: R.E., 3/200; L.E., 9/200. There was marked cataract formation and early dystrophic change in the corneal endothelium bilaterally.

In November, 1951, an attempted intracapsular cataract extraction was performed on each eye by a member of the resident staff. In the right eye a few lens remnants were left but these absorbed uneventfully in a few weeks; in the left eye all lens material was removed at the time of operation. Following operation vision in the right eye gradually improved over a period of one year

to 20/100, but thereafter failed progressively due to increasing endothelial changes. The left eye developed a generalized corneal haze one week following operation which never cleared; the vision in the left eye reached a maximum of 10/200 four months following surgery and thereafter began to fail due to increasing endothelial dystrophy.

In September, 1953, two years following cataract extraction, the vision had dropped to 5/200 in each eye. By April, 1954, the vision was recorded at 1/200 in each eye. There was marked endothelial dystrophy and pronounced corneal edema with some corneal scarring. Intraocular pressure measured 12 mm. Hg (Schiotz) bilaterally. At this time it was decided to perform keratoplasty.

On April 29, 1954, a 10-mm. posterior lamellar keratoplasty was performed on the left eye. The technique followed was the same as already described except that an air bubble was injected into the anterior chamber at the close of the operation.

Postoperatively the graft appeared clear and in good position. However, the air bubble became trapped behind the iris pushing the iris forward against the fresh edge of the graft and forming anterior synechias.

On the second postoperative day the intraocular pressure rose markedly. This was controlled by the use of Diamox and miotics and, even when these were discontinued, the tension remained normal for a period of four weeks. The tension again became elevated and required four operative procedures before finally responding: on June 8, 1954, a cyclodialysis was performed; on July 6th, cyclodiathermy was performed; on July 16th, a cyclodiathermy and posterior sclerectomy were performed; and on September 12th, a Stallard operation was performed. The tension thereafter has remained normal.

The vision immediately prior to operation was 1/200. Two weeks later the corneal edema had disappeared and the vision had risen to 5/200. With the repeated attacks of glaucoma and extensive glaucoma sur-

gery the vision dropped to its original level of 1/200 where it has remained.

One year following the operation corneal edema was still absent. The graft was in good position. Slight scarring at the graft interface was present, and scattered opacities were present in the recipient anterior cornea as had been present prior to operation. There was slight retraction of Descemet's membrane in a few places and some vascularization of the lower edge of the graft. Iris details could readily be seen through the graft.

COMMENT

The lack of visual success in this patient was due in part to the development of severe postoperative glaucoma after a large air bubble became trapped behind the iris. We can only speculate as to whether the visual outcome would have been more favorable had this complication not developed. The experience in this case does serve to show that this surgical technique is feasible. The graft has remained in good position and iris details can readily be seen through the graft

after one year. It is of interest that corneal edema, which was marked prior to surgery, has been absent for one year following surgery.

SUMMARY

1. A technique has been described for posterior lamellar keratoplasty.

2. A case of far-advanced Fuchs' endothelial dystrophy with aphakia has been presented in which this technique was utilized.

3. The postoperative course was complicated by a large air bubble becoming trapped behind the iris with resultant glaucoma. This was controlled after four glaucoma operations.

4. Vision prior to surgery was 1/200. This rose to 5/200 but later returned to 1/200 as a result of the prolonged glaucoma.

5. Corneal edema has been absent for one year following surgery and iris details are readily visible through the graft.

1511 Scott Avenue (3).

I wish to thank Mrs. Annette Burgess (Wilmer Institute) for the drawings illustrating the surgical technique.

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NONGRANULOMATOUS UVEITIS*

A COMPLICATION OF SERUM SICKNESS

RICHARD E. HOOVER, M.D.
Baltimore, Maryland

There is extensive experimental evidence¹ that nongranulomatous uveitis is a hypersensitive reaction and can be produced in animals through proper sensitization with either bacterial or protein antigens. There is extensive sound clinical evidence that nongranulomatous uveitis is usually dependent on an underlying bacterial hypersensitivity usually to one or more strains of the streptococci. It is peculiar, that so far as can be found, there is only one authentic report of clinical nongranulomatous uveitis due to hypersensitivity to protein agents. This is the report by Theodore and Lewson² of a patient who developed a nongranulomatous uveitis as a complication of serum sickness following the administration of an antipneumococcus serum.

Two quite similar cases have recently been observed in the Wilmer Institute, and are therefore reported as examples of nongranulomatous uveitis due to protein agents.

CASE REPORTS

CASE I

S. P., a 33-year-old coal miner, was an aerial gunner in the Army and had no eye difficulty until April, 1953, when he suffered a puncture wound of the left ankle. He was given 1,500 units of tetanus antitoxin and 600,000 units of penicillin immediately after the injury. Six days later, he developed severe urticaria for which he was hospitalized and treated. The urticaria subsided gradually. On the third day of this illness he noticed redness and aching of the left eyes. Two days later, the vision became hazy but it cleared during the next three days. This serum sickness reaction was not accompanied by joint pain or other manifestations. After

recovery he stated that once or twice per month he had transient attacks of blurring vision and redness of the left eye, each attack lasting for two or three days. In October, 1953, this dimness of vision persisted and he consulted an ophthalmologist. He was told that there was increased intraocular pressure, and was given hydrocortisone tablets and various topical medicine without improvement. He was first seen in the Wilmer Clinic in February, 1954. The right eye was never involved and remained normal at all times.

On examination, his right eye was normal with 20/20 vision. The left eye corrected to 20/20. There was no sign of active inflammation. The visual fields were normal. There were some old fine keratic deposits on the posterior surface of the left cornea of the lymphoid cell type. The aqueous ray was negative. The fundus was normal. The intraocular pressure measured 55 mm. Hg (Schiotz). The patient was hospitalized and a complete survey was done. There was no evidence of any granulomatous disease. Search for active infections was negative. Tests for bacterial hypersensitivity were negative except for a weak positive to two strains of the subgroup A of the beta streptococci. He was insensitive to B, C, and F subgroups and to the gamma streptococci. He showed a definite reaction to 30 units of intracutaneous tetanus antitoxin with three cm. of erythema and a one cm. central elevated blanched area surrounded by four or five small papules. Synchronous with this positive skin test the left eye flared with slight circumcorneal injection and a \pm aqueous ray. The patient was discharged to his local doctor with a diagnosis of secondary glaucoma following a nongranulomatous iritis, which complicated a serum sickness.

* From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and University.

CASE 2

A 32-year-old white woman was admitted to The Johns Hopkins Hospital on October 15, 1953, already ill with the classical picture of serum sickness. There was a history of migraine and a previous injection of tetanus antitoxin. Two weeks prior to admission, she had been exposed to diphtheria and eight days prior to admission had been given injections of penicillin and diphtheria antitoxin for a sore throat. Six days thereafter, and two days prior to admission she developed acute fever, general malaise, generalized lymphadenopathy, swollen painful joints, and erythematous rash. Treatment at the hospital consisted of intravenous fluids and pyribenzamine and adrenalin in oil, but these were not effective. She was then begun on cortisone and received approximately 350 mg. of the drug during the first 12 hours of treatment. Her response to this too was poor and she received an additional 350 mg. during the subsequent 12 hours. During that time, the adenopathy appeared to be less marked but she continued to have severe urticaria and edema. By the morning of the third day in the hospital she was much improved and at that time was being maintained on 50 mg. of cortisone every six hours. The usual adjuvant drugs were used. Her fever also remitted at that time and thereafter her temperature remained within normal limits. Over the next day or so her symptoms subsided; however, she did develop weakness of the shoulder muscles with winging of the scapula, diagnosed as a radiculitis, involving the nerve roots of the brachial plexus. During the latter part of the first hospital week, the drug was rapidly tapered until she reached a level of 100 mg. a day at which point she was discharged.

She returned on November 4, 1953, complaining of poor vision which she now dated from October 16th, one day after her former admission to the hospital. She was now referred to the Wilmer Institute for examina-

tion. There was a record of previous examination in November, 1951, at which time eyes and vision were normal. Examination showed corrected vision reduced to 20/40 in each eye. The eyes showed only a suggestion of circumcorneal congestion. The intraocular pressure was normal. The slitlamp examination in both eyes showed the aqueous ray to be negative. There were small keratic deposits of the lymphoid type scattered over the posterior surface of both corneas, and there was a liberal amount of fibrin in the anterior chamber and slight edema of the iris itself. No cells were seen.

The ophthalmoscopic examination in both eyes showed that the media were clear. The discs and macular regions were normal and no lesions were seen.

The diagnosis of nongranulomatous uveitis complicating serum sickness was made. The patient was treated with local hydrocortisone drops and when last seen on March 19, 1954, she had vision in the right eye of 20/20 and vision in the left eye of 20/15. The eyes were completely white. All keratic deposits had disappeared. There was no fibrin present. The intraocular pressure was normal. The irises were completely normal. Ophthalmoscopic examination was normal in all respects. She had made a complete recovery and as far as is known has had no recurrence since that time.

COMMENTS

In these two cases the etiology of the nongranulomatous iritis appears clear.

In Case 1, the occurrence of a focal reaction in the eye after a diagnostic test injection of the tetanus antitoxin would almost cement the diagnosis. The localization of the inflammation in one eye can readily be explained on the ground of any mild local trauma which is enough to fix preferentially the local antigen-antibody reaction.³

In Case 2 the sequence of events was typical and the nongranulomatous iritis was certainly part-and-parcel of the serum sick-

ness. The mild nature of the ocular reaction was interesting and we cannot but wonder if careful examination of the eyes of all patients with serum sickness might not show that uveal involvement is a common, rather than an uncommon picture.

The Johns Hopkins Hospital (5).

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OPHTHALMIC MINIATURE

It is known that the cause of fibromyoma is believed to be an estrogenic origin. That being the case, vitamin B complex deficiency appears to be the causative factor since the inactivation of the estrogenic hormone in the liver depends upon vitamin B complex. . . . The proper refractive correction is also essential due to the fact any existence of ocular parasympatheticotonia would lead to either reflex or voluntary gastro-intestinal parasympatheticotonia causing poor assimilation to the water soluble vitamin B complex, vitamin C, amino acids, and other metabolites. In two known cases to date, the correction of manifest myopia by another refractionist after refusing to abide to my concept of thinking of under-correction of myopia gradually lead to ovarian cysts of both ovaries one and one-half years later in one case and two years later in another case. In both cases the optometric manifestations were similar as mentioned above. The former patient is now under my attention periodically, reducing her state of myopia by reducing the state of anoxia, which was originally caused by overcorrection of myopia and nutritional deficiency.

(Well! Well! Ed.)

Joseph D. Sasaki, A.B., O.D.

"The optometric manifestations of hepatic carcinoma case,"

Michigan Optometrist, **34**: 8-9 (Sept.) 1955.

OPHTHALMIC RESEARCH

Department

EDITED BY FRANK W. NEWELL, M.D.

Abstracts of papers presented before the Western Section of the Association for Research in Ophthalmology, February 7, 1956, San Francisco, California

A. RAY IRVINE, JR., M.D., *Secretary, Western Section*

The energy requirements of the lens:

The ability of various metabolites to replace glucose as substrate. Daniel J. Heinrichs, B.S., and John E. Harris, M.D., Department of Ophthalmology, University of Oregon Medical School, Portland.

The energy requirements of the lens appear to be largely provided by the metabolism of glucose. Knowledge of the pathways of glucose metabolism in the intact structure is yet incomplete. The classic Embden-Myerhof anaerobic glycolytic sequence has been demonstrated. However, the pathways by which oxygen is utilized are not known with any certainty, although both the citric-acid cycle and the direct oxidative route have been postulated. One of the major obstacles to the direct study of this problem is the low oxygen uptake.

As an indirect approach we have studied an energy-utilizing mechanism, the cation pump, as an index of metabolic participation. When a lens is refrigerated at 0°C., potassium leaves the lens and sodium enters. During subsequent incubation at 37°C., potassium re-enters the lens and sodium is excreted from it. The relative ability of the lens to concentrate cations is considered to provide a measure of energy production. The cation pump has been shown to require oxygen.

In the present experiments the ability to replace glucose of certain metabolites known to be intermediate in the major pathways already mentioned has been

studied. Under the conditions of the experiment, we have found that small lenses may maintain a cation pump for some time without added glucose. Therefore, in these studies we have used lenses of a size that normally require added glucose. The substrates employed have included lactate, pyruvate, acetate, citrate, oxaloacetate, alpha-keto glutarate, gluconate, and ribose. None of the compounds tested were able to replace glucose as substrate. (Citrate proved to be quite toxic in the concentrations used, probably due to the binding of calcium, an ion which is essential for the maintenance of normal membrane permeability.)

The Excretion of Melanocyte-stimulating hormone by patients with certain ocular disorders.

John E. Harris, M.D., and Aaron B. Lerner, M.D., Departments of Ophthalmology and Dermatology, University of Oregon Medical School, Portland.

The melanocyte-stimulating hormone (MSH) is elaborated by the pituitary gland and can be found in detectable quantities in human blood and urine.* Under its influence the skin darkens. Urinary excretion of the hormone is decreased in pituitary failure and after the administration of corticosteroids. It is increased in adrenal failure probably due to the unchecked activity of the pituitary gland.

* Shizume, K., and Lerner, A. B.: Determination of melanocyte-stimulating hormone in urine and blood. *J. Clin. Endocrinol. & Metab.*, **14**:1491-1510, 1954.

This increase probably accounts for the pigmentation of Addison's disease. In certain instances, therefore, the melanocyte-stimulating hormone excretion can be taken as an index of the activity of the pituitary gland.[†]

Melanocyte-stimulating hormone excretion has been shown by others to be elevated in individuals with retinitis pigmentosa. We have confirmed this finding in a relatively small group of patients in whom this diagnosis was permissible and in whom varying degrees of visual disability were noted. In our series, while the majority showed an elevated excretion of the hormone, in some the amount excreted was within the normal range. There appeared to be no relationship between the visual disturbance or fundus picture and the melanocyte-stimulating excretion.

In one patient with a choroideremia the melanocyte-stimulating hormone excretion was elevated. However, the melanocyte-stimulating hormone output of his daughter, who showed a mottling of the pigment epithelium but no visual disturbance, was normal.

Melanocyte-stimulating hormone excretion was measured in a group of patients who, for various reasons, had had bilateral enucleations. These individuals showed a slightly elevated output, although the excretion was not as high as was encountered in many other disturbances.

The most interesting group proved to be the patients with diabetic retinopathy. The majority of these patients had an elevated melanocyte-stimulating hormone excretion. By contrast, a group of diabetic individuals without retinopathy showed a normal output. The melanocyte-stimulating hormone excretion appeared to be more related to the duration of diabetes than to the degree of retinopathy or the degree of control.

[†] Lerner, A. B., Shizume, K., and Bunding, L.: The mechanism of endocrine control of melanin pigmentation. *J. Clin. Endocrinol. & Metab.*, 14:1463-1490, 1954.

Bovine vitreous filtrate. A. Suran, M.D., and W. K. McEwen, M.D., the Francis I. Proctor Foundation for Research in Ophthalmology, University of California Medical Center, San Francisco.

Viscosity determinations on bovine vitreous filtrates at different age levels reveal an increase in viscosity with the growth of the eye. The possible filterlike action of the condensed outer layer of the vitreous was examined by permitting vitreous filtrate to drain through an exposed, undisturbed area of vitreous. Viscosities were measured on aliquots and it was found that the viscosities of the various fractions varied.

The viral etiology of epidemic keratoconjunctivitis. E. Jawetz, M.D., P. Thygeson, M.D., L. Hanna, M.A., S. Kimura, M.D., and A. Nicholas, M.A., Departments of Microbiology and Ophthalmology and the Francis I. Proctor Foundation for Research in Ophthalmology, University of California Medical Center, San Francisco.

A new member of the group of APC viruses has been isolated from a typical case of epidemic keratoconjunctivitis. Sera of patients with this disease show a striking rise in neutralizing and complement-fixing antibodies to this virus. The results of a serologic survey from three continents suggest that this new virus is regularly associated with epidemic keratoconjunctivitis as it occurred in 1951-1955.

Further studies concerning the activity of benzalkonium chloride against *Pseudomonas aeruginosa*. Sidney Riegelman and Daniel G. Vaughan, M.D., School of Pharmacy, Department of Ophthalmology, and the Francis I. Proctor Foundation for Research in Ophthalmology, University of California Medical Center, San Francisco.

It was recently reported by C. A. Lawrence that benzalkonium chloride (1:

5,000) is a highly effective bactericidal agent against *Pseudomonas aeruginosa*. Since this contradicted our own experimental results, tests were run in the Proctor Laboratory on four strains obtained from Dr. Lawrence. Using the corneal infectivity test we found benzalkonium chloride (1:5,000) to be lacking in its bactericidal effect against *Pseudomonas aeruginosa*. However, *in vitro* results were in agreement with the findings of Dr. Lawrence.

A bacterial retentive filtering procedure.

Sidney Riegelman and Daniel G. Vaughan, M.D., School of Pharmacy, Department of Ophthalmology, and the Francis I. Proctor Foundation for Research in Ophthalmology, University of California Medical Center, San Francisco.

A new filter membrane (Millipore Filter) incorporated in a Swinny filter adaptor has been proven to be completely retentive of bacteria and particulates of three microns or larger size. The assembly is attached to a hypodermic syringe, thus both filtering and sterilizing a solution with the application of a small amount of force on the plunger. This procedure is recommended as an additional safeguard in removing potential bacteria from an ophthalmic solution immediately prior to use in the eye during an operative procedure and in other dangerous situations. With the use of the present filter membrane, the authors question the retention of virus particles.

The technique of determination of blood volume changes in the choroid and retina. Victor G. Fellows, M.D., and J. W. Bettman, M.D., Stanford University, San Francisco.

Until the present time there has never been a technique for determining changes in the total blood volume of the choroid and of the retina. In the past there have been many attempts to evaluate effects on

the blood vessels. These include direct observations of the blood vessels of the retina with the ophthalmoscope, with or without a graticule, photography with a Nordenson camera, photography with a slitlamp and Koeppe lens, and observation through the scleral window according to the technique of Leopold. Other methods include indirect estimation of the effects of change in vascularity through use of the electroretinogram by the technique of Henke, measurements of flicker-fusion frequency, and angioscotometry. None of these techniques permit estimation of the total blood volume of choroid and retina.

The use of radioactive phosphorus permits a direct measurement of changes in blood volume of the choroid and retina. The radioactive phosphorus is incubated with red blood cells after a blood specimen has been drawn from the animal. Incubation and gentle agitation are carried out for two hours, the plasma and buffer coat are removed by centrifuging, and the red cells are resuspended in saline and reinjected into the animal.

Measurements of the radioactivity of the blood at intervals after such an injection indicate that the radioactive phosphorus remains in the blood stream for several hours. The vascularity of the sclera is negligible and that of the vitreous is nonexistent. Consequently, a Geiger-Müller tube placed over the sclera behind the ora serrata gives an indication of the blood volume under that tube. This blood volume is almost entirely contained in the retina and choroid.

Studies indicated great variation in blood flow unless there was control of the aeration of the animal. After intubating the animals and connecting them to a breathing machine, the results became constant. Variations in the carbon-dioxide and oxygen content resulted in changes in the blood volume.

An evaluation of agents influencing the blood volume of the choroid and retina.

J. W. Bettman, M.D., and Victor G. Fellows, M.D., Stanford University, San Francisco.

Using the radioisotope technique just reported, a systematic evaluation of agents which might affect the blood volume of the choroid and the retina was made. Certain vasodilators were entirely without effect; others seemed to constrict the blood vessels of the choroid and retina.

A new subconjunctival magnetic orbital implant. Orwyn H. Ellis, M.D., and O. Robert Levy, B.S., Los Angeles.

In co-operation with the Magnet Division of General Electric Company an implant containing a magnet, the active poles of which end directly under Tenon's capsule and conjunctiva, has been designed and produced. Since the magnetic force increases with the cube of the distance, to produce attraction, a magnet must be located as near as possible to the magnet in the prosthesis. This has been accomplished with this implant. The shape of the implant has been changed from a round back to a pyramid or cone. This has been found to rotate as well or better than the sphere, and has not turned in the orbit. The new implant appears larger but the volume is almost exactly the same. The movement of the finished prosthesis is as extensive or more extensive than that of previous implants, including the evisceration with implant.

Paper electrophoresis as applied to the study of aqueous humor or other dilute ocular fluids. Ernest K. Goodner, the Francis I. Proctor Foundation for Research in Ophthalmology, University of California Medical Center, San Francisco.

The problem of the concentration of dilute protein solutions and the detection of the several protein fractions by paper electrophoresis near or at the limit of the method was investigated. If the protein concentration of the specimen is not at

least 0.5 percent or higher, the presence or absence of the several globulin fractions cannot be definitely detected.

Lysozyme in the tears of rabbits. S. J. Kimura, M.D., Lynette Feeney, and W. K. McEwen, M.D., the Francis I. Proctor Foundation for Research in Ophthalmology, University of California Medical Center, San Francisco.

Ordinarily rabbit tears do not contain sufficient lysozyme to be detected by filter-paper electrophoresis. In a preliminary study it has been found that tears from an eye which is irritated or infected show lysozyme.

The protein components of human tears. Robert Brunish, Ph.D., Department of Physiological Chemistry, School of Medicine, University of California, Los Angeles.

Recently, McEwen and Kimura have employed filter-paper electrophoresis to separate the proteins present in tears. Their analysis showed the presence of at least three components in "normal" tears. One of these components was positively charged at pH 7.8 and was identified as lysozyme. Smollens, Leopold, and Parker, studying tears induced by a lacrimating agent, benzyl bromide, report the presence of four electrophoretic fractions, three of which were positively charged at pH 7.9. Caselli and Schumacher report the presence of five electrophoretic fractions, only one of which was positively charged at pH 8.6.

In order to resolve these differences and to study the effect of irritants upon tearing, different types of tears were compared using filter-paper electrophoresis and, whenever possible, the 2.0 ml. Tiselius cell of the Spinco Model H apparatus. The paper strips were analyzed by employing the protein stain, bromophenol blue, which was eluted and analyzed colorimetrically. Emotional tears and tears produced in excessive amounts presumably

through blockage of the nasolacrimal duct were considered "normal tears." No difference was found between these types of tears. The irritants used to produce tearing were freshly cut onions and Los Angeles smog. Since the effects produced by the two irritants were similar, the results represent a summary of the two. Although the globulins were resolved into two major and one minor components, they will be considered as one fraction.

The average of 21 "normal" tear samples showed a percent distribution as follows:

Albumin, 38.8 percent; globulin, 44.8 percent, and lysozyme, 16.4 percent. The 12 irritant-induced tear samples studied yielded values of 19.3, 54, and 26.7 percent. Exposure of normal tears to onion vapors did not change the composition suggesting that the irritant was not acting on the secreted fluid but was actually causing a different secretion to be formed. It is suggested that the changed secretions may reflect a mechanism comparable to that seen in the double innervation of pancreatic or salivary gland secretion by humoral and/or neural pathways.

Some useful characteristics of the accommodation and convergence hyperbolas.

Robert V. Hill, M.D., Department of Ophthalmology, University of Oregon Medical School, Portland.

Accommodation and convergence hyperbolic equations were derived mathematically and superimposed graphically for convenience of study of their normal and abnormal relationships. The common (and more solid) ground of an unequivocal mathematical expression of their normal relationships in all three variables (accommodation, convergence, and dioptric distance) provides a better background for study and discussion of abnormal relationships.

Fixation disparity in relation to heterophoria. Arthur Jampolsky, M.D., Ber-

nice Flom, O.D., and Allan Fried, O.D., Stanford University School of Medicine, San Francisco.

Fixation disparity may be defined as the amount by which the visual axes miss intersection at the point of regard during conditions of single binocular vision. Single binocular vision is a more general statement of the binocular fusional process but does not necessarily imply the more critical bifixation.

Fixation disparity, therefore, is true binocular fusion with inexact bifoveal fusion, the fusion being maintained by perifoveal and more peripheral fusional areas of Panum. It is as if the foveas "were sitting on edge" and fusion exists by "the skin of the teeth." Fixation disparity is an ocular deviation occupying an intermediate status between that of orthophoria with bifixation and a manifest strabismus.

It was the purpose of this study to measure fixation disparity in degree and character as it normally exists in patients exhibiting various degrees of heterophoria, under conditions simulating everyday visual situations. The experimental design had as its objective the binocular fusion of a large field of print with uniform peripheral as well as minute foveal fusionable detail. The error in exact bifoveal fusion (fixation disparity) was determined by an optimally designed vernier alignment technique, utilizing monocularly presented, oppositely polarized, lines at the fixation area. Special attention was given to avoiding induced visual stress by lenses or prisms in order to measure quantitatively the fixation disparity normally occurring in a variety of heterophorias. The target design used at all times allowed for the possibility of bifixation in that it is this error which was measured.

It was hypothesized that the magnitude of fixation disparity would not significantly vary with various degrees of exophoria, but would increase significantly and variably with increasing degrees of esophoria. This hypothesis was supported

by the evidence obtained in these experiments.

Ocular impedance, tissue heating, and scleral shrinkage in relation to electro-surgical treatment of retinal detachment.* Henry A. Knoll, Ph.D., Department of Biophysics, School of Medicine, University of California, Los Angeles.

In order to understand better the effects of electro-surgical treatment of retinal detachment on the eye, several fundamental aspects have been examined. Work to date has included measurement of ocular impedance at various frequencies, measurement of heat developed during the application of electro-surgical treatment, the shrinkage during the application of electro-surgical treatment, and the shrinkage characteristics of sclera and its effect upon intraocular pressure.

Impedance measurements have been made at six frequencies between and including 110 million cycles per second. Measurements were made on the eyes of anesthetized dogs and rabbits. The measurements were made before and after surface and puncture treatment. The results indicate little change in impedance after surface treatment but a drop in impedance after puncture. The drop is felt to be largely due to increased surface contact of the electro-surgical needle.

A thermocouple placed in the choroid and vitreous of the eyes of anesthetized rabbits was used to measure the temperature rise during electro-surgical treatment. In general the temperature gradient surrounding the needle is very steep and the heating effects are largely restricted to the external coats of the eye.

Strips of sclera and cornea from recently enucleated eyes of pigs and rabbits have been subjected to shrinkage measurements. Critical temperatures between 60° to 65°C. are indicated at which un-

loaded tissue will contract to approximately one half of its initial length. The tissue stretches only slightly upon return to body temperatures.

Changes in intraocular pressure as a result of electro-surgical treatment have been measured tonometrically in the eyes of anesthetized rabbits. Only a few surface treatments are required to double the intraocular pressure. Return to normal pressure required approximately one hour.

Observations on the anatomy of the trabecular meshwork as seen in tangential section. Milton Flocks, M.D., Stanford University, School of Medicine, San Francisco.

Increasing experimental evidence, suggesting that the trabecular meshwork is the site of increased resistance to aqueous outflow in open-angle glaucoma, has focused interest on the histology and pathology of this area.

The meridional sections commonly used in eye pathology show only a lateral view of the meshwork which does not reveal its basic anatomy. Tangential views of the trabecular apparatus have been described from tissue which had been teased from the eye but such descriptions have not been reported of sections of the meshwork made in situ. A simple technique of making tangential sections of the trabecula in situ has been devised. Using this method, a study of unused callottes from normal eyes of the Stanford Eye-Bank and of glaucomatous eyes from the Armed Forces Institute of Pathology and the Stanford University Eye Pathology Laboratory is being made. The anatomy of the meshwork is seen to be strikingly more complex than when seen in ordinary meridional sections.

The openings of the corneoscleral meshwork, in contrast to the uveal meshwork, have a definite shape and alignment which may have physiologic significance. The distribution of the trabecular cells and of enmeshed pigment is of interest.

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SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

December 16, 1954

DR. EDMUND B. SPAETH, *Chairman*

LEIOMYOMA OF THE IRIS

DR. WAYNE L. ERDBRINK, Lieut. (MC) U.S.N., Philadelphia, reported a case of a leiomyoma of the iris in a 20-year-old white man. The lesion was located in the inferior nasal quadrant of the left eye. The vision, intraocular pressure, and angle in the involved eye were normal. The clinical diagnosis was a leukosarcoma of the iris. Radioactive phosphorus (P_{32}) uptake studies were negative, indicating nonmalignancy of the tumor. The tumor was removed with a basal iridectomy and the patient has been followed for 10 months without evidence of recurrence. Pathologic examination of the tumor met the criteria for leiomyoma of the iris.

The world's literature was surveyed and 19 case reports were found. A summary of the historical and clinical characteristics of these cases and of the case reported here was made. Conservative surgical management of any case of a localized tumor of the iris was stressed.

Discussion. DR. JOHN MCGAVIC: I have had the opportunity of examining this patient clinically when he came to the Wills Eye Hospital for photographs and P_{32} studies. As we go along with this discussion, I think you will agree with me that the ophthalmic pathologist would welcome a divining rod like P_{32} as much as the clinician, because the microscopic diagnosis is sometimes almost as difficult as the clinical diagnosis. This patient's tumor fungated into the anterior chamber more than the usual leiomyoma, and did not show ectropion of the uvea, which is the rule. The literature says ectropion uveae

is present in about 35 percent of cases, but I think it is present much more frequently than this.

This slide shows a leiomyoma of the iris near the pupillary border. This type is thought to arise from the sphincter rather than from the dilator. This area represents a denser nuclear arrangement than the rest of the tumor. Associated with this there is a large cyst which lies between the two layers of epithelium on the posterior surface of the iris. In this instance, it extends into the pupillary area and was seen as a large dark mass. Some leiomyomas may be associated with dark masses, although they themselves are gray to yellow in color. This type of cyst is not uncommon in the published pictures of leiomyomas.

The first patient was a man about 40 years of age. The next one was the second case that the late Dr. Albert Frost found. He made the diagnosis clinically the second time. Incidentally his patient had glaucoma. I think we have had three cases with glaucoma that I know about as opposed to the one out of 20 cases reported by the essayist.

This slide shows a leiomyoma stained with trichome, and is the type that extends along the surface of the iris and tends to produce ectropion uveae. There is usually more ectropion than this. This patient was 28 years of age and had secondary glaucoma.

This is a slide of the case described by Moulton and Moulton. A man, aged 56 years, had an enlarging growth, noted for a year and a half, which measured five by seven mm., filled the anterior chamber, and pressed against the cornea. This case was mentioned by Dr. Erdbrink.

This next slide shows a low-power view of the globe with a leiomyoma involving the base of the iris and filling the angle, a situation which is said in the literature not to occur very often. We have two instances of

this. Secondary glaucoma is evidenced by the cupping of the nervehead.

This next case is one of those instances in which the glaucoma was rather acute. The cornea was steamy and vision was reduced to counting fingers at a few feet. The diagnosis of melanoma was made by three doctors, and leiomyoma by three others, so that you can take your choice. This is a slide to show you why the term fibroid is applicable to leiomyomas. You can see that the number of spindle-shaped fibrous cells here is quite marked and, as we look at the microscopic slides, you will see long, spindle-shaped cells which are quite different; the two parts may be present within the same tumor. This slide is from the same tumor, showing the spindle cells under higher power; the other part of the tumor showed the fibrous portion.

I have not seen this specimen before. I picked it up from the essayist just as we came in. It shows very well and looks as if it would be better than the ones we made. You can see that the cells are quite variable in their appearance. This is due in part to being cut in different planes. The cells are more or less spindle-shaped. Some of these appear round or oval but they are probably cut largely on cross-section. A lower-power view shows that some of the cells are really quite spindle-shaped.

This is a biopsy specimen in which all of the iris from here forward is involved by a tumor. There is a different type of cellular arrangement on the surface of the iris. The cells tend to spread along the surface of the iris, as epithelium is inclined to do.

I think this is the best picture of all, as far as showing the tendency for nuclei to palisade and to show spindle cells. A good many cells are spindle-shaped and appear even more so when you view them under the microscope; they grow in such different planes that it is hard to photograph them and show the spindle arrangement properly.

This next specimen is shown through the courtesy of Dr. James Shipman. The patient had a tumor of the lower portion of the iris,

which turned out to be a nevus as you can see by the nest of cells that are present. Now, in some of the published cases of leiomyoma, the photographs give you the impression that they may very well be nevus-cell tumors, and this would explain the difference in behavior of some of those cases. This is a higher-power view to show the arrangement of the nevus cells. You can see that they are more nearly rounded and oval rather than spindle-shaped, and that they are also arranged in nests.

This is a melanoma of the iris, which we felt was malignant. On section you notice it appears the same as leiomyomas. The cellular detail of melanoma can vary from the epithelioid type to a spindle-cell type. This is a malignant melanoma of the iris, involving also the ciliary body. It is nonpigmented. On section you could not tell it from a leiomyoma except under high power. There are other tumors which give the same appearance. This solitary tumor appears to be a leiomyoma of the iris; it has exactly the same appearance.

Melanomas of the iris are malignant in only nine or 10 percent of cases. Leiomyomas are only theoretically malignant. No proven case of metastasis from iris tumors has been reported. Only one leiomyoma has been reported from the ciliary body, and this one did not metastasize. We must agree with the essayist that removal of iris tumors by simple iridectomy, basal in type, is certainly the treatment of choice.

DR. I. J. EISENBERG: We have now been using P_{32} for almost three years. During this period approximately 10 to 12 iris lesions were tested by our technique. In this series there were two cases of malignant melanomas involving the iris and ciliary body, proven by histologic sections, which showed a positive uptake of P_{32} . We have also proven two cases of nonmalignant iris lesions which gave a negative P_{32} concentration. We also have four cases under observation. Everyone who has examined these lesions feels that they are so-called malignant

melanomas. Three of them show all the classical signs: encroachment of the angle, pigmented cells in the angle, and apparent increase in size; one case even showed destruction of iris stroma.

In these four cases the P_{32} test was negative. A possible explanation is that, even though these lesions show signs of malignancy by the established criteria, nevertheless they may not be true malignant lesions in the sense that metastasis will occur, and the metabolic rate may be no different from the surrounding normal iris stroma. This low metabolic rate and lack of clinical evidence of metastasis is further borne out by Reese's analysis of 32 proven cases of malignant melanomas of the iris, only three showed evidence of metastasis.

Our results and Reese's report raises a pertinent question in my mind as to whether or not lesions of the iris not involving the ciliary body should be considered to be clinically malignant, even if the pathologist reports a malignant melanoma. Only time and more facts will resolve this question. Nevertheless, from the information already known, I would like to urge a go-slow attitude for enucleation of an eye with a diagnosis of malignant melanoma of the iris.

CONGENITAL BILATERAL ABDUCENS

DR. JULES M. YASUNA and DR. NATHAN S. SCHLEZINGER reviewed the literature on Moebius' syndrome and presented two children, both of whom had congenital bilateral facial and abducens-nerve paralysis with retention of ocular convergence but little or no internal rotation of the eyes upon attempted lateral conjugate gaze. Associated anomalies consisted of a club-foot in one boy and a digital deformity of the hand in the other boy. Noteworthy in the comprehensive diagnostic survey of these two cases were: the absence of nystagmus and extraocular movements in response to caloric vestibular stimulation; the normal creatin and creatinine urinary assays; and the markedly reduced quantitative response observed in the

electrical muscle reactions of the face. Exploratory operative surveys in both cases revealed grossly normal lateral rectus muscles with free movement of the eyes in response to forced duction maneuvers. The muscle biopsy was reported as showing some abnormality in the form of a loss of striation and a peripheral migration of the nuclei in some of the fibers, but these changes were not marked and were considered as not consistent with dystrophy but probably consistent with a relatively slight degree of muscle atrophy.

On the basis of the data obtained in the study of these two children, it is postulated that Moebius' syndrome is a result of a congenital brainstem lesion which is predominantly supranuclear in its effect upon the abducens nerve and either nuclear or infranuclear in its effect upon the facial nerves.

Discussion. DR. HOWARD BEDROSSIAN: Henderson, in 1939, reported 61 cases of this syndrome; abducens palsy was present in 45. Out of those 45 cases, 23 showed a convergent squint. The other 22 had straight eyes.

In reviewing the literature concerning this syndrome, I think one of the most interesting features is the pathology postulated for these cases by two schools of thought: (1) There exists a primary aplasia of the muscle due to a mesodermic defect, and (2) there is a nuclear or ectodermal defect.

Evidence of muscle defects have been shown by Shenkle, Obersteiner, McDonald and Mittendorf and Heuck.

The most outstanding of these reports is the one by Heuck, in 1897, of a family in which the mother and three children had eye muscle defects, including bilateral ptosis, inability for outward movement of either eye, as well as no ability to elevate or lower the eyes. One of the children died at the age of 18 years, and the autopsy specimen showed that all except the medial rectus muscles were inserted abnormally posteriorly, as much as 2.5 mm. in some, and that nearly all the muscles were too short, as much as 10

to 11 mm. short in the case of the inferior rectus muscles. He concluded that the faulty insertions and incomplete development adequately explained the defective motility. The nerves were not examined.

Those favoring the theory of a nuclear or ectodermal defect suggest two main types of nuclear involvement. One type is aplasia of the nuclei. Heubner's case report in 1900, which Dr. Schlezinger mentioned and which is quoted in Duke-Elder's and in Walsh's textbooks, is an example of this type. Degeneration is the other type of nuclear involvement, as shown in a case reported by Lanny and Fowler, in 1903, of a patient who had facial diplegia but no ocular involvement. Pathologic examination showed degenerated nuclei, nerves, and atrophied muscles. Other authors, such as Spatz and Ullrich, and Balint have also reported nuclear pathologic processes.

The possibility that two different types of pathology may exist is nicely summarized in a very interesting article by Leszynsky, in 1897. He stated that, in the few cases examined post mortem, there has been found either complete absence of the muscle or abnormal insertions. "Neuropathology teaches that fibrous degeneration and complete absence of a muscle may be due to a primary nuclear atrophy; while on the other hand, the nuclear atrophy may result from a loss of function or atrophy of muscle."

I would like to present a case, in addition to Dr. Schlezinger's three cases, which is an example of muscular pathology.

Mr. N. D., aged 35 years, complained of inability to gaze laterally since birth. Previous medical history was that of a left herniorrhaphy and spinal arthrodesis at the ages of 16 and 18 years. Visual acuity was correctible to 6/6 in each eye. Ocular movements showed ability to elevate and depress the eyes normally. He was unable to abduct or adduct either eye. Convergence was present with normal pupillary reactions. His near-point of convergence was 20 cm. from the nose. Bell's phenomenon was present.

The patient showed first, second, and third degree fusion in eyes front. His prism divergence was 10/5 and convergence 20/10. Opticokinetic nystagmus on the rotating drum test showed no response on either side. He had a slightly masked facies, but there was no real definite facial paralysis. He was able to smile but not quite as normal individuals. He showed diminished hearing on the right, a hammer toe on the right, and, in his family history, a cousin had webbed fingers.

A Bárány test was performed at another institution, and the report suggested a midline infratentorial lesion. In view of this finding, Bárány and caloric tests were repeated at the Graduate Hospital. The report of the consultant was as follows:

"Hypoactive reflexes to both mass caloric and Bárány testing. Bárány testing is of decreased value because of lack of nystagmus. However, if the patient's eye complaints are on the basis of intracranial pathology, such pathology would be located in the midline to coincide with decreased response to vestibular stimulation."

The patient was operated upon but, before surgery while the patient was under anesthesia, a forced duction test was performed. We were not able to abduct or adduct either eye at all, but we could easily elevate and depress the eyes with the forceps. The medial and lateral rectus muscles were then explored and found to have many check ligaments. Tenon's capsule in the region of the muscle insertions was about as thick as the muscle itself. The lateral rectus muscle was inserted 12 to 13 mm. from the limbus. The medial rectus muscles were also inserted slightly more posteriorly than normal. An attempt was made to stimulate the muscles directly by electricity while the patient was under anesthesia. Both alternating and direct currents were used in the usual manner, but no response was obtained. The technician performing the electrical stimulation felt that no conclusions could be drawn because the patient was under anesthesia. Postoperatively

no improvement whatever was obtained in abduction or adduction, although the muscles were freed without being detached.

In summary I would like to make the following comments:

1. In view of the questionable facial diplegia, this case may not be a typical example of Moebius' syndrome, nevertheless it could be classified with that group of congenital anomalies.

2. The pathologic process in this case is definitely peripheral in the muscles.

3. It is hoped that, in the future, more cases of this type will be recognized, and that forced duction tests and exploration of the muscles will be performed for diagnosis. If this is done, then future correlation of muscular aplasia with nuclear aplasia may be obtained.

4. A knowledge of existing peripheral congenital ocular muscle pathology will help prevent misinterpretation of vestibular tests in suspected brain-tumor cases.

DR. FRANCIS HEED ADLER: The question whether this is a muscular dystrophy or a nerve-tract lesion is of real importance. Since these patients retain convergence, and yet have no adduction of either eye on versions, it is likely that we are dealing with a lesion of the posterior longitudinal bundle. One might argue, however, that the failure of the right eye to adduct in levoversion, and of the left eye to adduct in dextroversion, is merely due to lack of training, since a child with a congenital bilateral sixth-nerve palsy will have no occasion to use the medial rectus of the opposite eye in versions.

This argument is plausible, since we see it under other circumstances. In children with congenital ptosis, for example, one frequently finds failure of the eyes to move upward on command after the lids have been manually elevated, merely because the child has never used upward gaze. After some practice and urging, the eyes will turn up, demonstrating that the muscles for sursumversion are not paralyzed.

In certain forms of strabismus, the habit-

ual squinting eye may not abduct, and give rise to the appearance of a sixth-nerve palsy, but, after the fixing eye has been patched for a week or so, abduction is regained. This, however, cannot be the case here, since we find that the medial recti do not work in versions, no matter what the stimulus.

It is well known that these patients do not show any horizontal optokinetic nystagmus, nor any horizontal nystagmus as the result of vestibular stimulation—Bárány chair or douching the ear. In spite of this, they retain good convergence, which proves to me that these cases must be due to lack of development of nerve tracts involving the sixth and seventh nuclei and the posterior longitudinal bundle.

DR. I. J. EISENBERG: Dr. Adler, in the involvement of the sixth nerve are there cases with esotropia?

DR. FRANCIS HEED ADLER: Oh yes, I think only about half as I recall, have esotropia; in others, the eyes are straight in the primary position.

DR. NATHAN S. SCHLEZINGER: I do not believe there is anything to add except that I am wondering how a muscular disorder postulated in the case mentioned by Dr. Bedrossian could explain cases in which there was also facial involvement. In other words, we cannot consider facial paralysis a consequence of some abnormal insertion of the muscle, but rather a result either of myopathy or nuclear dysplasia.

BLEPHAROPHIMOSIS

DR. EDMUND B. SPAETH reviewed the history of this rather difficult type of ophthalmic plastic surgery and discussed the basic anatomic pathology to illustrate the essential requirements for correction of the defect.

Epicanthal folds with the basic defects, when these lie largely in the lower lids, are most difficult to correct. Dr. Spaeth presented a new operation for the correction of this so-called epicanthus inversus—a term which he thinks rather superfluous. The operation, which has no great technical difficul-

ties, was based upon the satisfactory correction of over 70 cases. The entire paper was published in *THE AMERICAN JOURNAL OF OPHTHALMOLOGY* (January, 1956).

William E. Krewson, 3rd,
Clerk.

NEW ENGLAND
OPHTHALMOLOGICAL
SOCIETY

January 19, 1955

DR. FRANK W. DIMMITT, *presiding*

The afternoon session of the 422nd meeting of the New England Ophthalmological Society consisted of the presentation of several interesting clinical cases followed by a Pathology Conference conducted by Dr. Taylor R. Smith. In the evening session, after the business meeting, two original papers were presented: the first, a case presentation, by Dr. J. D. Houghton, Chief of the Laboratory Service for the Veterans' Hospital in Boston; and the second, a paper on "Success or failure in glaucoma surgery," by Dr. P. Robb McDonald of Philadelphia.

SOLITARY METASTASIS OF RENAL-CELL CARCINOMA

DR. J. D. HOUGHTON: A 63-year-old night watchman of French-Canadian extraction claimed to have been struck by a light steel chain over a point in the angle between the bridge of the nose and the right eyebrow in November, 1953. Allegedly, a lump appeared at this site two weeks later, and slowly underwent painless enlargement, spreading upward over the forehead.

In January, a pulsating bruit from this area became audible to the patient, and there was slight downward displacement of the eye and diplopia.

Following angiography, a right external carotid ligation was done and the bruit ceased but, after four weeks, enlargement of the

tumor was resumed and the bruit returned.

By May 12th, a palpable, pulsating, moderately firm, low, bulging mass about 8.0 by 6.0 cm. was present over the right medial forehead, extending down over the brow ridge. The edges of a defect in the frontal bone could be felt after emptying the tumor of blood by steady pressure. The globe was pushed anteriorly and to the side, with marked diplopia in all directions of gaze. Fundus was normal and vision 20/20. Impression, after additional arteriograms, was cirroid aneurysm.

Excision of the mass was performed on August 5th. The tumor was about 11.5 cm. long (vertically), 5.5 cm. wide, and 0.5 to 0.6 cm. thick, encapsulated anteriorly, and bulging from the anterior table of the frontal bone. It was pink-gray, pliable, tough, and highly vascular, with profuse bleeding at operation.

Histologically it showed solid nests of clear cells compartmented by capillaries and slightly larger vascular spaces. This architecture closely resembled that of carotid-body tumor, and together with the lack of lumen formation or of fat or glycogen in the cells led to a diagnosis of chemodectoma or nonchromaffin paraganglioma. Since the tumor was alleged to be primary in the orbit, it was presumed to have arisen in the ciliary paraganglion described by Botar and Pribe (in a chimpanzee).

Additional sections of tumor taken from the specimen five months later revealed lumen formation, which is not found in chemodectoma. Accordingly, renal-cell carcinoma was suspected. Following an intravenous pyelogram, the right kidney was removed on January 28th. It contained a large tumor mass, the whole weighing 550 gm. Large areas of it were histologically identical with the tumor in the frontal bone and orbit, leaving no doubt that the latter was a metastasis.

It should be emphasized that at no time since onset had the patient noted the slightest symptom referable to the genito-urinary tract, although the renal tumor must have

been present for at least a year and two months. At this time, two months after nephrectomy, there is still no evidence of any other metastasis.

Only one case (Fisher and Hazard; *Cancer*, 5:521, 1952) and two other possible examples (Lattes, McDonald, and Sproul; *Ann. Surg.*, 139:382 [Mar.] 1954; Pendergrass and Kirsh; *Am. J. Roentgenol.* 57:517 [Apr.] 1947) of chemodectoma of the orbit have been reported in the literature. The first case was followed for only three months after operation. In each of the other two there was a coexistent carotid-body tumor, raising the possibility that the orbital tumor was metastatic. No ciliary paraganglion has ever been reported as found in a human. In view of the experience here described, it would seem advisable not to report further examples of this entity, if indeed it exists at all, without benefit of bilateral renal exploration or complete autopsy.

SUCCESS OR FAILURE IN GLAUCOMA SURGERY

DR. P. ROBB McDONALD, pointed out that the numbers and variations and types of glaucoma operations merely emphasize what a complex picture we are attempting to reduce to a common denominator, namely, elevated tension. He cited progress in research which has given us a better understanding of the problem as a whole, and proceeded with the discussion of surgery for different types of glaucoma.

He considered four groups of glaucoma which are usually subjected to surgery: Acute congestive glaucoma, malignant glaucoma, chronic glaucoma, and congenital glaucoma.

Acute congestive glaucoma was considered to be the most satisfactory to treat, and operation is the treatment of choice except in unusual cases. It was further advised that the other eye should be given a prophylactic iridectomy. He stated that a short trial of medical treatment (about three to six hours) should be given in a case of acute glaucoma and then surgery should be resorted to.

A peripheral iridectomy with a tight wound closure was recommended for all cases which can be controlled medically, or when one can be sure it is the first attack. Wound closure was emphasized to promote speedy formation of the anterior chamber and to prevent converting the glaucoma into a chronic type. Also selection of a suitable area for the iridectomy was mentioned since it had been observed that polycoria in some instances produced troublesome diplopia when the iridectomy was below the upper lid margin, even though the tension was well controlled.

Complications and failures he attributed to faulty history and examination, in which chronic glaucoma is mistakenly treated as acute narrow-angle glaucoma, although he added that even in chronic glaucoma peripheral iridectomy works well if the tension is controlled by miotics. The second cause for failure, from the patient's point of view, is injury to the lens by a keratome or iris forceps, thereby producing a poor visual result.

Malignant glaucoma was described as essentially that glaucoma in which there is a narrow angle, in which the pressure cannot be reduced to normal, and in which one gets virtually no aqueous on making a section or entering the anterior chamber. The iris diaphragm is displaced forward and the eye stays hard even after the anterior chamber has been opened. He pointed out that this poses a real problem to the surgeon as to whether to proceed with cataract extraction at that time, or whether to perform a peripheral iridectomy and see if the chamber will reform. In case cataract extraction is performed he re-emphasized the fact that it is desirable, in this type of case, to lose vitreous by incising the hyaloid if vitreous is not lost spontaneously, and added that, in a case in which malignant glaucoma has been known to exist in one eye, a prophylactic peripheral iridectomy in the other eye is highly advisable.

In discussing the problem of chronic glaucoma, Dr. McDonald pointed out that a

peripheral iridectomy is good only when the tension can be controlled by miotics; otherwise, a filtering operation is needed. The relative merits of trephination and iridencleisis were discussed, and it was pointed out that trephination is usually a more difficult operation, the danger of hypotony is greater, iritis occurs more frequently, the bleb is usually larger, and when cataract forms, it comes on more rapidly. Also there is greater chance of late secondary infections than with the iridencleisis. However, with iridencleisis, results are usually not very good when the tension is very high.

A late complication of trephination is the possibility of acute hypotony. Dr. McDonald discussed opinions as expressed by Kronfeld regarding the increase of outflow by filtering operations as against the evidence presented by DeVoe that in many cases there is successful surgery with no evidence of filtration by gonioscopy. He felt that, probably, DeVoe had been dealing with a group of narrow-angle glaucomas which had been cured by the iridectomy and had no need for fistulization. An extremely large filtering bleb was definitely considered an undesirable result, and the speaker suggested that the large bleb usually develops in those cases in which Tenon's capsule has not been sutured at the time of the operation.

In congenital glaucoma, the operation of choice was considered to be goniotomy, if the diagnosis is made early. The speaker pointed

out that if goniotomy is done in conjunction with goniotomy, one should be careful not to make the puncture too large for fear of prolapse of the iris. It was also pointed out that, in many congenital glaucoma patients, the iris tissue cannot be adequately stripped from the angle and kept back. When cyclodiathermy is used for congenital glaucoma, the results may be unpredictable.

Discussion. DR. PAUL A. CHANDLER chided Dr. McDonald for astutely recognizing a "misery case" and referring him to Dr. Chandler. He stated that, after five operations, the tension was still up. This case was used to illustrate the point that, in many instances, the technique does not seem to make much difference; that even though operations seem to go very satisfactorily, and from a technical point of view would seem to have everything in their favor, there is some "X" factor which determines whether the patient will get a satisfactory reduction in tension. He agreed with Dr. McDonald's analysis of DeVoe's series, and considered the patients that were cured without filtration had cases of narrow-angle glaucoma. He stated that in the cases of open-angle glaucoma "no filtration—no cure." He agreed that iridectomy should be done if the glaucoma is controlled by drops, and that also if it is the first attack, an iridectomy will work even if the drops have not brought the tension down.

David H. Scott,
Recorder.

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ALAN CHURCHILL WOODS

Ther nys noon so good a physician as
thy trewe freend. *Chaucer.*

This number of THE JOURNAL is in honor of a great ophthalmologist, teacher, and friend, Alan C. Woods, professor emeritus of ophthalmology of The Johns Hopkins University, who retired from active academic

teaching on July 1, 1955. It is a festival writing, or *Festschrift*, a happy custom long established by our Germanic colleagues. The contributors are former students and fellow members of his faculty. They adopt this way of expressing their admiration, nay affection, respect, and gratitude to one to whom they owe so much that is good in inspiration, skill, and training. The rest of us are beneficiaries,

for these contributors are the leaders of American ophthalmology.

Alan Woods is a man of many facets. There is no need here to discuss his numerous contributions to our science. We all know their importance and have been benefited unmeasurably by them. There is no need to detail the many honors that have been given him, most justly, for these important contributions. There is no need, also, to list the high offices in our profession that he has filled with great distinction. This is not, thank the Lord, an obituary.

Elliott Randolph, who had the job of collecting these papers, which he has done very well indeed, has in this issue, written a most delightful and deeply affectionate tribute to the "Professor." I cannot add to that intimate and delightful sketch, from the viewpoint of Alan's group. Few of us, indeed, have been privileged to be so intimately associated with him in his daily work, and to witness the hourly expression of his skill and character.

The rest of us have had to judge Alan from seeing and hearing him at our formal meetings, reading his many scientific contributions, and a few of us fortunate ones, conversing with him in most informal surroundings where he set the pace of good fellowship. The judgment by all is good, and we have learned to love him as a man of great integrity, forthrightness, courage, learned acumen, but above all of friendly humor and good companionship.

Those of us in the family of *THE JOURNAL* take great pride in the fact that he is one of us. We have leaned on him on many occasions of uncertainty and doubt, and he has never failed us in assistance and wise counsel. We consider it a great honor to ourselves to be able to render him this tribute of affectionate respect.

All of us join in wishing Alan Woods many more years of fruitful productivity for our patients' benefit and our own. We selfishly hope that he will be spared us many years of cheerful companionship. We all

wish him well on this occasion of his retirement from years of active teaching, and look forward in the years to come to what we have become accustomed to, his guidance and sterling leadership.

Derrick Vail.

V PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

The fifth congress of the Pan-American Association of Ophthalmology opened in Santiago, Chile, on Sunday, January 8th, and closed on Saturday morning, January 14th. It was a very good meeting indeed. Two hundred and thirty-six members registered as follows: Argentina 41, Bolivia 5, Brazil 21, Mexico 4, Nicaragua 2, Paraguay 5, Peru 12, Puerto Rico 2, Panama 1, El Salvador 1, Uruguay 6, Venezuela 5, Ecuador 2, Cuba 6, Colombia 3, Canada 3, United States of America 114, Ireland 1, Spain 1, France 1. The headquarters for the meeting and exhibitions was the modern and comfortable Hotel Carrera, the facilities of which were quite adequate for our purpose.

Santiago is a beautiful city, rapidly becoming modernized, lying in a plain about 100 miles from the coast. This being their summer, the days were hot but the evenings and nights delightfully cool. The surrounding mountains, some of which are snow-capped, gave a framework of great beauty. Parts of old Santiago left over from Spanish colonial days are still standing and serve to enhance the romance of the place. Two large hills, San Lucia and San Cristóbal, erupt from the center of the city and are parklike landmarks beloved by natives and visitors alike. The surrounding countryside, composed of rich farmlands and vineyards, was surprisingly verdant for this time of year.

The congress opened with an appropriate and glittering ceremony in the gemlike Municipal Theatre. The Minister of Health, Sr. Raúl Barrios Ortig, gave us a gracious welcome, and was followed by several speak-

ers; Macoyr E. Alvaro, our courageous president, A. Edward Maumenee, Jorge Balza, and Hilton Rocha; then came the address of the president of the V Congress, Cristóbal Espildora Luque. After this, a brief and moving tribute to Dr. Carlos Charlin and to Chilean ophthalmology was held at the ophthalmologic clinic of the El Salvador Hospital, followed by a delightful Chilean luncheon at the School of the Carabineros. The members of the association then had the choice of attending a special exhibition of horsemanship by the "Cuadro Verde" or selected cavalry, where they were well rewarded with thrilling examples of trick riding and jumping, or going to the Sunday horse races at the beautiful and elaborate "Club Hipico" and venturing their pesos on their fancy, especially in a race named in honor of the congress. The directors of the club gave a tea to the delegates and, from all accounts, everyone enjoyed himself, even the losers.

The scientific sessions began promptly on time on Monday, January 9th, and continued daily through Friday, January 13th. The only respite was an opportunity for a two-hour siesta during the day, except for Wednesday when a special barbecue luncheon with appropriate refreshment copiously provided, was held in the country at the Viña Undurrago (Santa Ana). This was a truly delightful fiesta held under lovely old eucalyptus trees, which provided adequate shade to the fruit and flower-bedecked tables. The food, fruit, and drink were delicious. Native singing and dancing accompanied the feast, and it was with considerable regret that we had to tear ourselves away from this joy to return to a late afternoon scientific meeting, which a surprising number did.

The program was well arranged, although perhaps too generously. Official symposia were held on collagen diseases, primary glaucoma, infantile glaucoma, secondary glaucoma, retinal detachment, psychosomatic ophthalmology, tropical diseases, physiopa-

thology, and surgery of the lens, plastic surgery, fields and neuro-ophthalmology, and intraocular tumors. Besides these, there were sessions devoted to the Association for the Prevention of Blindness, and a large number of free papers. In all 92 papers were scheduled. A number of authors found themselves unable to attend but their places were filled in by others who were not on the official program.

On Wednesday morning, January 11th, a session of the Chilean Society of Ophthalmology was held in the Hall of Honor of the University of Chile. The president of the society, Dr. Alberto Gormaz, gave an address of welcome. The third Harry Gradle Lecture was given by Dr. Frederick C. Cordes of San Francisco (in absentia) whose title was "Residency training in ophthalmology." Then followed a tribute to Dr. Carlos Charlin by Dr. Gunther von Grolman, a lecture by Dr. H. Arruga on "Opportunity and selection of the operation of retinal detachment," a lecture on "Surgical treatment of infantile glaucoma," by Prof. Edmond Velter of Paris, France, and an address by Dr. F. S. Lavery of Dublin, Erie, on "Orthoptic exercises." The session concluded with a distribution of diplomas to the new members, corresponding and honorary, of the Chilean Society of Ophthalmology.

On the whole the scientific papers were of excellent quality and a few of them outstanding. A novel and successful arrangement had been made to translate simultaneously the remarks of the speakers into English and Spanish, as the case might be. It worked remarkably well, and, as a result, the attendance at the meetings, even during the long and late hours required to cover the ground, was exceptionally good. A large measure of the credit for the success of this effort should go to the interpreters who did a remarkably good job and, I suppose, were the most fatigued of all of us when the meetings were over. There is no room here to give a detailed description of the nature and extent of the papers presented but, for-

tunately for all of us, these will be published as an *Acta* in the very near future.

In addition to the scientific programs, scientific films were shown daily, and this seemed to be the most popular feature of the whole scientific part of the congress. In all 29 films, mostly of surgical interest, were shown. Some of them were particularly noteworthy. There was also an excellent scientific exhibit which was well attended in the few off moments.

The Gold Medal of the National Society for the Prevention of Blindness was presented to Dr. Luis Sánchez Bulnes of Mexico for his notable work in this field by President Alvaro. It was a most popular choice of a recipient for this high honor that is given only every four years.

The closing banquet of the congress was held in the beautiful and elaborate Union Club of Santiago on Friday evening, January 13th. The spacious halls were crowded and the delicious banquet was followed by short, gracious, witty, and effective speeches. Dancing to the music of an excellent Chilean orchestra then ensued.

The officers of the association for 1956-1960 will be:

President, Brittain F. Payne of New York; honorary executive secretary-treasurer, Thomas D. Allen; executive secretary-treasurer for north of Panama, Wesley McKinney; executive secretary-treasurer for south of Panama, Jorge Balza. Assistant secretary-treasurers: John Matthews, A. E. Maunee, Alfred Elliott, Edward McKay, Charles Bahn, Paul Craig, John McLean, Daniel Snyder, Michael Hogan, A. B. Reese, Pedro F. Gracia Nocito (Argentina), Alcides Del Ciello and Renato de Toledo (Brazil), Guillermo Pico (Puerto Rico).

Vice-presidents: Argentina, Baudilio Courtis; Bolivia, Aniceto Solares; Brazil, Hilton Rocha; Canada, Henri Pichette; Chile, Santiago Barrenechea; Costa Rica, Alexis Aguero; Colombia, Jorge Arango; Cuba, Miguel Branly; Ecuador, Juan Durango Lopez; El Salvador, Humberto Esca-

pini; Guatemala, R. Pacheco Luna; Haiti, Elie Villard; Mexico, Raul Chavira; Panama, Benjamin Boyd; Paraguay, Honorio Camouzano; Peru, Jorge Valdeavellano; Puerto Rico, Ricardo Fernandez; United States, William L. Benedict and Derrick Vail; Uruguay, Antonio Debezies; Venezuela, Rodolfo Hernandez Miliani.

A new and special post was created, that of executive director, for the retiring president of the association, Maocy E. Alvaro. This was a most wise decision for it thereby ensures the continuing of the valuable services of this remarkable ophthalmologist and linguist who has done so much to bring the ophthalmologists of North and South America together for the good of the cause. His unique knowledge of the special problems and characteristics of ophthalmology throughout this hemisphere truly make him an indispensable servant and leader, especially during these formative and struggling years.

The Chilean ophthalmologists worked hard and long for the great success of this congress, and all of us admire their skill and congratulate them for the brilliant result attained. The meetings were run with admirable precision and suitable decorum, the physical arrangements were most satisfactory, and the generous entertainment, both private and official, left nothing to be desired. We all departed from Santiago with much regret but with joyful and grateful memories that will survive in our hearts for many years to come.

The next congress (VI) of the Pan-American Association of Ophthalmology will be held in Caracas, Venezuela, in 1960. The exact date has not yet been established.

Derrick Vail.

CORRESPONDENCE

GRAECO-LATIN WORDS

Editor,

American Journal of Ophthalmology:

To one who has frequently been offended by the misspellings and misuses of Graeco-Latin words in the ophthalmic literature, but did not have the courage to protest for fear of being branded a pedant or a show-off, it has been refreshing and gratifying to read the letter of Dr. Sidney Fox in the October, 1955, issue of *THE JOURNAL*. The knowledge of not being quite alone in this feeling of offense encourages me now to give vent to one of my pet peeves.

Distichiasis is, indeed, a hard word. One can hardly expect a latter day ophthalmologist to recognize the difference between stichos and thrix. Classical education is no longer a requirement for entrance into medical school. But most men have had a little smattering of it, worse luck. And they know, therefore, as who doesn't, that the ending in -a denotes the feminine singular. So they write, and the editors print, that the *media* is clear, the *data has been* collected, and so on with *phenomena*, *criteria*, *acta*. The trouble is, of course, that the ending in -a is not always feminine singular, but may be neuter plural. The *media* of the eye include more than one medium, the *data* reported—one hopes—more than one datum. One can't always be sure whether the author refers to one phenomenon (or criterion) or to two or more phenomena (or criteria), but one can be confident about the meaning of *acta*.

Basically there is no reason why these words in their form in -a could not be used as *pluralia tantum* (as we were taught to call them in my childhood), words of plural form but constructed in the singular. If this is generally agreed—and there are precedents: the news is either good or bad or indifferent—all objections stop, for correct grammar is simply best usage.

The difficulty is that not all words in -a are

Latin singular feminine or pleural neuter. To compound the difficulty—and the offense—they may be Greek singular neuter. It hurts the few who still know this to hear *Erythema nodosum* called *nodosa*. But even those who are hurt must realize the fact that the important thing is to recognize the erythema for what it is and that it makes very little difference to the patient whether his erythema, carcinoma, or glaucoma, is Latin singular feminine or Greek singular neuter.

(Signed) Hermann M. Burian, M.D.,

Iowa City, Iowa

BOOK REVIEWS

ADVANCES IN OPHTHALMOLOGY. Volume IV. Edited by E. B. Streiff, Basel, Switzerland, S. Karger, 1955. 328 pages, 42 illustrations, mostly in color. No index. Price: 39.50 Swiss francs.

Volume IV of this excellent series is now available. It is equal to, or even surpasses, its predecessors, which have proved to be of such value to us all in the past. The subjects covered are "Orbital implants," by Dr. P. Choyce of London; "Gonioscopy" (in French), by J. François of Belgium; reviews on "Physical optics and dioptrics," by M. C. Colenbrander of Leyden; "Teratology of the eyes" (in German), by P. J. Waardenburg of Leyden, who has also written the chapter on "Embryology of the eyes"; and "Cornea and sclera" (first part), a review of the literature from 1946-1951, by S. Forni of Geneva (in French). There are some beautiful illustrations in color by François. His article is particularly noteworthy and practically a textbook on the subject.

Dr. Choyce's article on orbital implants conclusively shows that the integrated type has not held up with the passage of time. All of us who have done this operation are aware of this fact by now. In a way it is a sad chapter in ophthalmic surgery and shows what happens on premature reports of these "quickies." We should profit by this experience.

Volume IV of the *Advances in Ophthalmology* is most worthy of its predecessors. All should be in the library of every ophthalmologist.

Derrick Vail.

TREATMENT OF AMBLYOPIA (*Amblyopiebehandlung*). By Dr. Alfred Bangerter. Basel, S. Karger, 1955 (second edition). Cloth bound, 144 pages, 44 illustrations, several tables. Price: 18 Swiss francs.

The late Joseph I. Pascal reviewed the first edition of *Amblyopiebehandlung* in this space in November, 1953 (*Am. J. Ophth.*, 36: 1637). At that time, neither the author nor "pleoptics," the term he had chosen for his method of visual training, had any familiar ring in American ophthalmologic literature. Only two years later, any discussion of amblyopia invariably includes references to this Swiss ophthalmologist and his sensational claims for his treatment of amblyopia.

Bangerter differentiates true amblyopia from relative amblyopia. The former includes cases with and without strabismus. Relative amblyopia comprises cases of high degrees of myopia, of nystagmus, and instances of congenital or acquired anomalies of the refracting media, the retina, or the optic nerve. They are classed as "relative" because the organic changes are not severe enough to account for the markedly reduced vision.

It is Bangerter's opinion that amblyopia is a developmental anomaly rather than suppression of an already developed function. Consequently, his method of treatment is based on that assumption. This is one of the reasons why he reserves occlusion for only a relatively small number of cases, where his ideal form of treatment can be carried out.

The fundamental considerations on which the various steps of treatment are based are (1) establishment of conditions most favorable to vision (particularly correction of refractive errors and surgery in high degrees

of strabismus), (2) use of adequate stimuli, (3) utilization of the interrelation between central and peripheral vision, (4) utilization of the interdependence between both eyes, (5) association of other sensory functions with the process of vision, (6) utilization of mnemonic factors, and (7) utilization of the fact that moving targets can be recognized more easily than stationary ones.

It is extremely tempting to describe in some detail how Bangerter realizes these principles in practice. However, for the purpose of this review, suffice it to say that he employs a score of instruments, most of them of his own design, and most of them extremely elaborate.

In Bangerter's own "Sehshule," this equipment is housed in a building close to the St. Gallen Eye Hospital; it is under the latter's administration. In addition to the medical director and his medical associate, the personnel consists of the chief orthoptist, the administrator, three trained orthoptists, and seven student orthoptists.

It would seem difficult to duplicate such an ideal set-up. Only institutes with enormous resources could plan to organize a pleoptic school that would offer facilities similar to that in St. Gallen. Out-of-town patients have to stay at the school for from eight to 12 weeks, if their amblyopia is high. Patients within commuting distance undergo the training in about the same span of time, with two visits a week. Daily visits are required only for the establishment of central fixation; that particular period of the training extends through three or four weeks.

The clinical material consists of about 400 cases. Unfortunately, the results are summarized so vaguely that they are almost useless for statistical purposes. Even the author admits that some of his results are disappointing.

It is an accepted fact that "amblyopia ex anopsia" can be influenced therapeutically; hence, it is entirely possible that Bangerter's method (or for that matter, any method using an approach more active than usual)

may produce speedier and, possibly, more impressive improvement than the rather passive approach that is the standard treatment today. Without first-hand knowledge of the system of Bangerter, it would be highly unfair to judge or condemn many of the new ideas he proposes.

When it comes to his concept of "relative amblyopia," it seems that Bangerter treads on extremely dangerous ground. Not less dangerous is his interpretation of some of his results. To cite an example, a seven-year-old boy with advanced optic atrophy due to Crouzon's disease had an initial visual acuity of finger counting at one meter. After 58 sessions of pleoptic training, that vision had improved to R.E., 0.15; L.E., 0.2. While it might be argued in the author's favor that enthusiasm carries him away in the interpretation of his results, one cannot be as charitable when discussing some suggestions he makes regarding preventive measures to stop the progress of myopia; Bangerter advocates a series of retrobulbar injections with hypertonic saline solution, combined with daily pilocarpine instillations.

To create conditions most favorable for binocular vision, Bangerter recommends lens extraction in cases of unilateral high myopia, followed by injections and pleoptic schooling. It is not clear from his discussion whether he has actually performed scleral shortening to reduce myopia or whether he merely toys with that idea. A combination of lens extraction and scleral shortening seems to belong to the realm of speculation, at least for the time being.

The subject of the book under review is highly thought-provoking. There is no question that the author is a sincere and original thinker. But one cannot but feel that enthusiasm for his subject has caused a certain loss of judgment. Only when other researchers carry out independent investigations on a similarly large scale will it be possible to gain a clearer idea of this controversial subject. But what institution has the resources to build a Sehschule on the scale of St. Gallen,

and how many patients can afford to undergo such an intensive treatment?

Stefan Van Wien.

AS I SAW IT. By Robert B. Irwin. New York, American Foundation for the Blind, 1955. 205 pages, index. Price: Not listed.

This book presents a remarkable survey of recent accomplishments in handling the special problems of the blind. Its brilliant author died in 1951 before the volume was ready for press. As a tribute to his dynamic leadership this posthumous publication is graced with a personalized title, substituted for the original designation, *Fifty Years of Progress*, which aptly summarized its content. The biographic allusions in the brief editorial comments that preface each of the 10 chapters give a fascinating glimpse of the author's amazing career. Though totally blinded at the age of five years, Dr. Irwin attended the Universities of Washington and Harvard, won as his wife a beautiful sighted girl, and became nationally recognized for his outstanding work as supervisor of classes for the blind in the public schools of Cleveland (1909-1923). In 1923 he was invited by the American Foundation for the Blind, which had been organized just the year before, to be its director of research and education, and in 1929 he became its executive director. For years his name was practically synonymous with that of the institution.

In 1905, five distinct codes of embossed print were used in this country. The confusion was not resolved for years. Irwin was a ringleader in the establishment of Standard English braille for all English-speaking countries in 1932. A method of stamping braille on both sides, called interpointing, was introduced in 1925 and has lessened the bulk of braille volumes by 40 percent. The phonograph, as an aid for the blind was mentioned by Edison in his first patent application in 1877, but nothing was done until it became a WPA project in 1934 at Irwin's suggestion. Today there are over 35,000 users of *Talk-*

ing Books as compared with some 9,000 braille readers.

Through Irwin's efforts the blinded and their guides can travel for a single fare; and a congressional act was passed favoring government purchase of products made by workshops for the blind. During the war millions of pillow cases were made for the military services, and three shops displayed proudly the earned "E" flag for excellence.

Heart-stirring indeed are the manifold ventures of the American Foundation for the Blind and the pageant of inspired, devoted persons who have made this a better world for the blind to live in, so ably unfolded in these pages.

James E. Lebensohn.

THE CORNEA. By Charles I. Thomas, M.D. Springfield, Illinois, Charles C Thomas (no relative), 1955. 1,318 pages, 400 figures, references, index. Price: \$30.00.

This book measures $6\frac{1}{2}$ by $9\frac{1}{4}$ by $2\frac{1}{2}$ inches and weighs six pounds. The type we are told is Caledonia, set 11 point on 13 point, and the text paper, which is superb, is 70 lb. Warren's Lustrum Glass enamel. The illustrations are likewise superb and the bookmaker has done a fine job of it all.

The author is associate clinical professor of ophthalmology, Western Reserve University, School of Medicine. He is particularly known in ophthalmology for his early and significant work on keratoplasty and, for this reason, his chapters on this subject are particularly good.

The author has done an enormous and valuable work of reading, collating, editing, sifting, and collecting all the significant works in the literature in most all languages pertaining to the cornea in health and disease. As such his text will stand as a classic, particularly for reference. Would you know about the anatomy, embryology, physiology,

pathology of the cornea? It is all here. Would you care to study the methods of examination, congenital anomalies, dystrophies, infections, manifestations of general and contagious diseases and skin diseases, and lesions from metabolic and allergic origins? Here they are. Tumors, pterygia, and injuries are likewise covered. The chapters on the treatment of all these things are as complete as is humanly possible. It is a super-colossal achievement and fills one of our urgent needs. We congratulate the author and publisher for a fine piece of work and are grateful to them for making it available.

Derrick Vail.

INDIAN YEAR BOOK OF OPHTHALMOLOGY, 1954. Edited by V. D. Sathaye (member) Poona University Court. Published in Poona (India) 502 Narayan Peth, 1955. 194 pages, index, supplement containing a directory of the eye specialists in India. Price: Not listed.

It is a pleasure to welcome the appearance of this ophthalmic reference work in English. The editor, an internationally known ophthalmologist, has skillfully accomplished his purpose of gathering together in a handy volume selected reviews of abstracts of the main articles in ophthalmic literature for the year 1954.

It is hoped that this venture will be successful and expanded to include editorial comments and criticisms so that what is good can be emphasized and retained, and what is not good can be critically examined and discarded.

This volume and the new *Journal of the All-India Ophthalmological Society* show us that Indian ophthalmology is coming of age in its own right and promises much for the future.

Derrick Vail.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tensor
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

I

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Kato, Y. **A morphological study of myoepithelial cells in human lacrimal gland.** *Acta Soc. Ophth. Japan* 59:1780-Nov., 1955.

From morphology, Kato classified the myoepithelial cell (basket cell) of the human lacrimal gland into star-cell, spindle-cell and transition forms. She further describes the distribution of the cell in the gland and discusses the functional role of the cell in lacrimal secretion. (35 figures, 23 references) Yukihiko Mitsui.

Lazorthes, G., Pigassou, R., and Gaubert, J. **The pathway of the intrinsic nerve fibers of the third nerve. An anatomical and pathological study and tentative conclusion on the pathogenesis.** *Bull. Soc. belge d'oph.* 109:16-23, Feb., 1955.

The diagnostic value of monocular mydriasis has been known for a long time but the theories concerning the pathogenesis of this sign have been numerous and contradictory. Anatomic and pathologic studies have shown that the nerve fibres supplying the intrinsic eye muscles are partly unprotected and easily pushed towards the

posterior clinoid process. Serial sections of the third nerve, stained with Kiss' osmic acid stain proved the independent structure of these nerve fibres and their location on the nasal superior border of the third nerve. This exposed location makes them susceptible to injury in damage of the posterior clinoid process and posterior cerebral artery and posterior communicating artery.

A pertinent case history is reviewed. A 65-year-old woman had cranial trauma with loss of consciousness and right-sided mydriasis. The autopsy revealed contusion of the frontal and temporal lobes, a break through the superior part of the clivus and a complete separation of the posterior clinoid process which was only supported by the dura mater. (4 figures, 3 references)

Alice R. Deutsch.

Rohen, J. **"Sperrarterien" (arterial sphincters) in the choroid and around the papilla in the dog.** *Arch. f. Ophth.* 156:90-97, 1954.

A number of photographs show "Sperrarterien" supplied with special muscle cells of the intima. This type of blood-vessel seems to have a special function in regulating the blood circulation of the choroid. However, neither in men nor in

rabbits and cats could similar mechanisms be detected. (6 figures, 15 references)

Ernst Schmerl.

Rossi, Antonio. **Morphology of the normal vitreous studied by electron microscopy.** *Rassegna ital. d'ottol.* **24**:215-232, May-June, 1955.

With the electron microscope one observes artefacts and normal formations in the vitreous. As artefacts Rossi considers the gross, rounded amorphous structures and some fibrous formations. The small, isolated bodies are probably united protein micromolecules and some of these remain isolated, whereas others become grouped and form fine fibrils, similar to collagenous embryonic fibers. Artefacts are probably due to dehydration. (15 figures, 18 references) Eugene M. Blake.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Biegel, Albert C. **Experimental ocular effects of high-voltage radiation from the betatron.** *A.M.A. Arch. Ophth.* **54**:392-406, Sept., 1955.

Changes in rabbit eyes following exposure to 16 to 19 mev electrons and 23 mev X ray by means of the betatron are described. Cataractous changes were noted four to six months after doses as low as 225 r. (12 figures, 4 charts, 1 table, 37 references) G. S. Tyner.

Hayashi, Y. **Findings of the optic nerve in experimental acute disseminated encephalitis.** *Acta Soc. Ophth. Japan* **59**:1429-1432, Sept., 1955.

This study is similar to that of Kabat and others (*J. Exp. Med.*, **89**:295, 1949). Hayashi demonstrated in rabbits that the brain tissue had an autosensitizing capacity to produce acute disseminated encephalomyelitis, as Kabat and others did in monkeys. The clinical result was posi-

tive in three of 37 animals. There appeared a palsy and ataxy of the legs three to ten weeks after an injection of brain emulsion plus adjuvant. The brain had been obtained from the same animal from the anterior lobe of the brain. After onset of the clinical symptoms, the animals were killed for histology. By histology, a demyelinating change was demonstrated in the central nervous system along with some cellular infiltrations. (9 figures, 1 table, 5 references) Yukihiko Mitsui.

Horwich, H., and Fedukowicz, H. **Variations in the Morax-Axenfeld diplobacillus.** *A.M.A. Arch. Ophth.* **54**:580-585, Oct., 1955.

Laboratory studies by the authors demonstrate the variable morphology of the Morax-Axenfeld bacillus. Variants are indistinguishable morphologically from anthrax bacillus, staphylococcus and others. (20 figures, 8 references)

G. S. Tyner.

Nishi, T. **Diseases of the eye caused by sensitization and provocative injection with egg white in rabbits; injection into anterior chamber, vitreous body and retrobulbar space.** *Acta Soc. Ophth. Japan* **59**:1666-1675, Oct., 1955.

Nishi injected white of egg into the anterior chamber, vitreous and retrobulbar space of rabbits sensitized with the same agent. The injection into the anterior chamber and vitreous resulted in the onset of an acute nonpurulent iridocyclitis. The posterior portion of the uvea was preserved even after repeated intravitreal injections.

Repeated retrobulbar injections caused a retrobulbar optic neuritis and finally a retinochoroiditis at the posterior pole of the eye. (10 figures, 3 tables, 55 references) Yukihiko Mitsui.

Waldrott, G. L., Hanser, S. A., and Theodore, F. H. **Symposium: Ocular al-**

lergy. *Tr. Am. Acad. Ophth.* **59**:474-500, July-Aug., 1955.

Waldbott, George L. **Ocular allergy from the allergist's point of view.** pp. 474-479. The author reviews briefly the various ocular allergic manifestations, particularly with reference to treatment. He considers lid edema, dermatitis, blepharitis, conjunctivitis, keratitis, cataract, uveitis, glaucoma, and some retinal conditions from the standpoint of etiology, elimination, desensitization, counteracting infection and treatment.

Hanser, S. Albert. **Laboratory studies in ocular allergy.** pp. 480-489. Hanser discusses such diagnostic procedures as 1. conjunctival scrape smear, including the method of preparing and examining slides, and 2. diagnostic anterior chamber puncture. He also discusses drug intolerance. (6 tables, 38 references)

Theodore, Frederick H. **Differential diagnosis of external diseases on an allergic basis.** pp. 490-500. Theodore mentions allergies of the ocular tissues, allergies to drugs and cosmetics. He gives a practical discussion of the differential diagnosis of external ocular allergies based on general basic allergic ideas and clinical and experimental experiences. (4 tables, 16 references)

Theodore M. Shapira.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Alajmo, Arnaldo. **Histamine content of subretinal fluid in retinal detachment.** *Gior. ital. oftal.* **8**:289-291, July-Aug., 1955.

Histamine was found in the subretinal fluid in three of four cases of detachment of the retina.

V. Tabone.

Auricchio, Giacinto. **Effect of uveitis on the water and amino acid content of the lens.** *Gior. ital. oftal.* **8**:242-250, May-June, 1955.

The effect of uveitis on the water and amino-acid content of the lens was studied in seven rabbits. It was found that first the water content of the lens increased, but later decreased both relatively and absolutely. The determination of the contents of amino acids under the same conditions was not reliable, as results were irregular and difficult to interpret. (1 figure, 2 tables, 26 references) V. Tabone.

Auricchio, Giacinto. **Effect of uveitis on the alkaline reserve in the lens and in the intraocular fluids.** *Gior. ital. oftal.* **8**:251-254, May-June, 1955.

The results of several experiments showed that inflammation of the uvea produced a lowering of the alkaline reserve of the lens and of the intraocular fluids. (3 tables, 10 references)

V. Tabone.

Bounds, G. W., Janes, R. G., and Leinfelder, P. J. **Cataracts induced by alloxan diabetes in rats and rabbits.** *A.M.A. Arch. Ophth.* **54**:564-572, Oct., 1955.

The progression of cataracts in alloxan-diabetic rats could not be influenced by the administration of nicotinic acid, cysteine or oxygen. The progress of the cataracts was related to the severity of the diabetes. (4 figures, 1 table, 14 references)

G. S. Tyner.

Bruce, Gordon M. **Permanent bilateral blindness following the use of hexamethonium chloride.** *A.M.A. Arch. Ophth.* **54**:422-424, Sept., 1955.

A 34-year-old negro woman with hypertension became permanently blind after the use of this drug. Visual loss resulted within a few minutes after intramuscular injection of 6 mg. The appearance of the fundi simulated acute ischemia. (19 references)

G. S. Tyner.

Capalbi, S. **The action of Prednisone (Metacortandracin) on the anaphylactic**

keratitis of the rabbit. Arch. di ottal. 59: 409-415, Sept.-Oct., 1955.

Prednisone inhibited experimental anaphylactic keratitis when given directly after the sensitizing injection, and reduced its intensity when given after keratitis had been produced. (9 references)

John J. Stern.

Capalbi, S., and Andreani, D. **Prednisone (Metacortandracin) in ophthalmology.** Arch. di ottal. 59:423-433, Sept.-Oct., 1955.

In 36 patients with various disorders, ranging from spring catarrh to uveitis, Prednisone was administered in a 1-percent ointment and in 5 mg. tablets. When both eyes were affected, one eye was given cortisone as a control. Prednisone seemed to have a more rapid and more potent effect, and was particularly effective in cortisone-resistant conditions. (2 tables, 20 references)

John J. Stern.

del Castillo, Caballero. **The hypophysis and the eyeball.** Arch. Soc. oftal. hispano-am. 15:637-658, June, 1955.

The influence of the eye, as a receptor of light stimuli, in the production of the melanophore hormone is discussed, and the author's experimental data reported. In order to determine the effect of light transmitted through the eyeball on the production of the melanophore hormone the author confined to darkness the following groups of frogs: normal frogs, hypophysectomized frogs, frogs with both eyes enucleated, frogs blinded by section of the optic nerves close to the chiasma, and hypophysectomized frogs with enucleated eyes. The hypophysectomized frogs whether blind or not lost their skin pigment, while not hypophysectomized blind frogs with enucleated eyes, or with section of the optic nerves retained their skin pigmentation. This proves that the eyeball is not the only factor stimulating the production of the melanophore hor-

mone. In these blind frogs there appeared to be an increase in melanophore production. A parallelism between the depigmentation of the skin and of the iris was noted in hypophysectomized frogs, indicating that the iris is also under the influence of the melanophore hormone. Further experiments consisted in the implantation of fragments of hypophysis or hyophyseal extracts into the anterior chamber of hypophysectomized toads; the result was a dense repigmentation limited to the iris of the eye in which the implant was made. This stood out in marked contrast to the depigmented iris of the control eye. The intensity of repigmentation and its duration varied according to the melanophore content of the tissue introduced into the anterior chamber. The hemato-aqueous barrier apparently checks the diffusion of the melanophore hormone into the general circulation, as long as the concentration is not very high. Only in cases with marked melanophore concentration in the anterior chamber did the effect manifest itself beyond the eye, in the skin of the experimental toads. The author points out that implantation of tissue into the anterior chamber can be utilized as a biologic test for the presence of melanophore hormone. The other tests for melanophore hormone are reviewed and the superior possibilities of this procedure pointed out; the iris of the fellow eye can serve as a control; it permits the identification of slight changes; and affords a quantitative comparison of the degree of repigmentation. Such a test thus appears to have qualitative as well as quantitative possibilities. (5 figures, 21 references) Ray K. Daily.

Centanni, Leonardo. **Difference of behavior of the succinic dehydrogenate-oxidate of some tissues and those of the retina and its relation to cortisone.** Rassegna ital. d'ottal. 24:269-280, July-Aug., 1955.

The author refers to his previous work

concerning metabolic enzymatic processes in the retina and their correlation with cortisone. He now attempts to apply these tests to other than ocular tissues, such as brain and liver, employing the manometric method of Warburg. The hypothesis is proposed that the activity of the dehydrosuccinic factor shown in the retina provoked by cortisone treatment has an indirect inhibitory mechanism, thus explaining the catalytic action of succinic acid. (5 tables, 13 references)

Eugene M. Blake.

Centanni, L. **The metabolic action of compound E (cortisone) on the normal retina of the rabbit.** *Boll. d'ocul.* **34**:460-477, Aug., 1955.

The author briefly reviews the literature concerning the oxidative-reductive processes of the retina. From his own work he concludes that the reduction of the dehydrogenase activity of the normal retina following the retrobulbar injection of cortisone may be due to the inhibitory action of cortisone on intermediate cellular metabolism. (56 references)

William C. Caccamise.

Citroni, Mario. **Polarographic research of the consumption of oxygen by the lens.** *Rassegna ital. d'ottal.* **24**:183-193, May-June, 1955.

Citroni was able to determine the biological characteristics of the crystalline lens by a new microanalytic technique. Polarographic determinations of the oxygen in the rat's lens were made under diverse conditions. Experiments showed the advantage of the electrolytic method as compared with the manometric. The former showed greater sensitivity and the possibility of determining the consumption of oxygen in the presence of other gases or substances which interfere with the precision of the gas-volumetric method. (3 figures, 2 tables, 39 references)

Eugene M. Blake.

Cook, C., and Ashton, N. **Studies on developing retinal vessels. III. Role of sympathetic innervation in oxygen vaso-obliteration.** *Brit. J. Ophth.* **39**:626-628, Oct., 1955.

The authors use 12-day-old kittens to show that the vaso-obliterative effects of oxygen on immature retinal vessels is uninfluenced by cervical sympathectomy. No immediate or delayed influence could be ascertained, nor could this be modified when Dibenamine was given as an adrenergic block. These findings concur with those of Patz. (8 references)

Lawrence L. Garner.

Davson, Hugh. **Adsorption of thiocyanate to the plasma proteins—with special reference to the distribution of this ion between aqueous humour and plasma.** *Brit. J. Ophth.* **39**:681-684, Nov., 1955.

The author discusses the findings of Kinsey and Palm who in 1955 described the kinetics of penetration of the sodium and thiocyanate ions into the aqueous humor. The latter felt that the cyanate ion penetrated by diffusion while the sodium ion was secreted by the ciliary body. Davson believes that a re-evaluation of these studies will reveal that there is no great fundamental difference in the mode of penetration of these two ions. This does not mean that they are identical, but simply that present techniques of study are not of sufficient delicacy. The author suggests that the results of Kinsey and Palm be re-computed. (1 figure, 6 references)

Lawrence L. Garner.

Dische, Z., and Zelmanes, G. **Polysaccharides of the vitreous fibers.** *A.M.A. Arch. Ophth.* **54**:528-538, Oct., 1955.

90 to 95 percent of vitreous matter consists of a fibrous, extractable, complex polysaccharide material. Other materials found in the vitreous are polyuronide, soluble glycoprotein and hexosamine. (1 figure, 3 tables, 19 references)

G. S. Tyner.

Dorello, U. **Electrophoretic studies of the protein content of the subretinal fluid in idiopathic retinal detachment.** Arch. di ottol. **59**:416-422, Sept.-Oct., 1955.

In 16 cases a high protein content was observed, without relation to the age of the detachment. The higher the protein content became, the more the electrophoretic picture resembled that of plasma. It is concluded that the protein in the subretinal fluid derives from the blood. (12 references) John J. Stern.

Ezuka, K. **Studies on adenosine triphosphate in the retina. III.** Acta Soc. Ophth. Japan **59**:1788-1793, Nov., 1955.

This is a chemical study in a homogenate of frog retina. A tracer, radioactive P^{32} , was used for the analysis. Ezuka concludes that the retina has a capacity to compose organic phosphoric acid by synthesis. The capacity is greater in the dark than in the light. The synthesis increases by an addition of glucose, $MgCl_2$ and adenosine triphosphate; it decreases by 2,4-dinitrophenol and mono-iodo-acetic acid. (4 tables, 23 references)

Yukihiko Mitsui.

Gloster, J. **Investigation of the carbonic anhydrase content of the cornea of the rabbit.** Brit. J. Ophth. **39**:743-746, Dec., 1955.

The author investigates the presence of carbonic anhydrase in the rabbit cornea. Its presence has already been reported in the lens, ciliary body and iris. A manometric method of extraction was employed but no evidence of carbonic anhydrase activity was found. (2 tables, 8 references) Lawrence L. Garner.

Hallett, J. W., Naib, K., and Leopold, I. H. **Control of experimental herpes simplex virus keratitis.** A.M.A. Arch. Ophth. **54**:572-579, Oct., 1955.

Hormonal, vaccine and antibiotic therapy were ineffective in control of experi-

mental herpes simplex virus keratitis. (7 figures, 11 references) G. S. Tyner.

Ito, N. **An experimental study on vascularization of the cornea.** Acta Soc. Ophth. Japan **59**:1693-1700, Nov., 1955.

Ito produced a pannus in rabbits by an injection of alloxan into the corneal stroma or into the anterior chamber. A pannus was also brought about in young rabbits by feeding an ariboflavinous diet. He made his observations by biomicroscopy as well as by biopsy. The first sign of pannus formation was a dilatation of limbus vessels. Then there appeared a cystic aneurysm. Cellular infiltration in the surrounding tissue, with a loosening of the corneal stroma, was associated with it. (14 figures, 29 references)

Yukihiko Mitsui.

Kaneko, K. **Respiration of the retina measured by Cartesian diver manometry.** Acta Soc. Ophth. Japan **59**:1713-1718, Nov., 1955.

This is a study of the retinal respiration in rats which are kept in a high altitude. Animals are killed soon after a stay in a high altitude and then the respiration of the retina is measured by manometry. According to Kaneko's measurement, no change in the retinal respiration takes place below 4,000 meters inclusive. A slight decrease in the respiration occurs at 5,000 meters after a ten hours' stay. At 7,000 meters, a decrease in respiration can take place in the periphery of the retina after a five-hours' stay, but only after a ten-hours' stay in the center of the retina. At 8,000 meters, the decrease occurs after five hours either in the center or in the periphery of the retina. (6 tables, 12 references) Yukihiko Mitsui.

Kinoshita, Jin H. **Carbohydrate metabolism of lens.** A.M.A. Arch. Ophth. **54**:360-368, Sept., 1955.

A study and evaluation of aerobic pathways of carbohydrate metabolism of the

lens is reported. The metabolism of glucose in the lens proceeds mainly by the glycolytic mechanism. However, the aerobic phase of glucose metabolism in the lens is different from that of other tissues. The production of carbon dioxide from glucose is largely effected through the direct oxidative pathway, with little participation by the citric acid cycle. The possibility of an alternate process for the reoxidation of reduced TPN is presented. (5 figures, 5 tables, 21 references) G. S. Tyner.

Kozawa, N. **The influence of thiamin-deficient diet on the vitamin B₁ content of the retina.** *Acta Soc. Ophth. Japan* 59: 1608-1614, Oct., 1955.

In the normal chicken the vitamin content in blood, retina and optic nerve is 8.7, 203.3 and 139.0 percent on the average respectively. When the chickens are fed with white rice, a clinical sign of vitamin deficiency begins to appear after one week. After 17 to 20 days the vitamin B₁ content in the tissues mentioned above decreases to 3.0, 119.5 and 116.5 percent respectively. When vitamin A, B₂, B₆ and C are added to the white rice, the decrease of vitamin B₁ in the retina and optic nerve becomes slightly more pronounced in the same period of time. This may be due to an increase in the metabolism of the body by those vitamins, which cause an increase in the consumption of vitamin B₁. An administration of vitamin B₁, 0.5 mg. daily for three days, does not cause a complete recovery from the deficiency in either case. (5 tables, 42 references)

Yukihiko Mitsui.

Lipetz, Leo E. **The X-ray and radium phosphenes.** *Brit. J. Ophth.* 39:577-598, Oct., 1955.

The author reviews the literature dealing with this subject and attempts to draw conclusions as to the mechanism by which these radiations arouse a visual sensation. This paper is the first of two dealing with

this subject and presents a critical review. The second paper, to be published at a later date, will attempt to test the conclusions drawn at this time. On the basis of the present review, arguments and evidence are submitted ascribing X-ray phosphene to a breakdown of the photochemicals in the rods and cones of the retina by the ionizing action of the rays. Radium phosphene is thought to consist of two phosphenes; one caused by the beta particles from the radium, while the gamma particles produce a much dimmer reaction. The gamma rays probably act by breaking down the photochemicals in the rods and cones. (123 references)

Lawrence L. Garner.

Mayer, G. **Hyaluronidase in ocular tissues. Sensitive biological assay for small concentrations of hyaluronidase.** *Brit. J. Ophth.* 39:747-750, Dec., 1955.

A very sensitive method for determining the presence of extremely small quantities of hyaluronidase is described, using the principle of modified decapsulation of bacteria. (5 figures, 10 references)

Lawrence L. Garner.

Muenich, William. **Effects of heparin and ACTH upon the uptake of radio-phosphorus by the calf's cornea in vitro.** *Arch. f. Ophth.* 156:119-126, 1954.

Heparin is probably best known for its inhibitory effect upon blood coagulation. The author enumerates numerous other qualities. He used heparin, ACTH and both substances together in his experiments on the corneal uptake of P³². Heparin increased the uptake of radioactive phosphorus, ACTH did not show a definite effect. When both substances were simultaneously administered the P³² uptake seemed to be diminished. (2 tables, 45 references)

Ernst Schmerl.

Nakamura, M. **Metabolism of crystalline lens, effect of inhibitors on respira-**

tion and glycolysis of the lens. *Acta Soc. Ophth. Japan* 59:1658-1666, Oct., 1955.

This is a part of the extensive study of the lens by Uyama and his collaborators. The present author considers that Embden-Meyerhof's glycolysis and Krebs' cycle play a role in the metabolism of the lens. The following facts obtained by him seem to corroborate this conception. Pyruvic acid and lactic acid in cultivated lens decrease by an addition of mono-iodoacetic acid, sodium fluoride and glycerine-aldehyde; and they increase by NaCN and malonic acid. The increased pyruvic acid by malonic acid decreases again by an addition of fumaric acid. Pyruvic acid increases also by adenosine triphosphate and decreases by co-carboxylase. (6 figures, 6 tables, 9 references)

Yukihiko Mitsui.

Nover, Arno. **The function of the lacrimal gland in the rabbit.** *Arch. f. Ophth.* 156:177-190, 1955.

The author continued his studies dealing with the regeneration of the lacrimal gland and found that normal rabbits, in comparison to man, secrete only small amounts of lacrimal fluid. Intravenous injections of thyroxin increased the secretion of the lacrimal material. Newly formed glandular tissue seemed to be able to produce and secrete lacrimal fluid. The author feels that his findings confirm vom Hofe's clinical observations that treatment with thyroid hormone may be of value in keratoconjunctivitis sicca and similar conditions. (9 figures, 25 references)

Ernst Schmerl.

Nover, Arno. **Regeneration and transplantation of the lacrimal gland exposed to local and general hormonal stimuli (thyroxin).** *Arch. f. Ophth.* 156:98-118, 1954.

The author studied regeneration in situ and regeneration of transplanted parts of

lacrimal glands in a large number of rabbits under general or local administration thyroxin. He found that regeneration was accelerated where thyroxin was given intravenously. (12 figures, 1 table)

Ernst Schmerl.

Orzalesi, F., and Miglior, M. **Effect of serum protein on the permeability of the lens capsule to glucose.** *Gior. ital. oftal.* 8:202-212, May-June, 1955.

Using various techniques, the authors showed that the presence of serum proteins retarded the permeability of the posterior lens capsule to glucose. They ascribe this both to the oncotic pressure of the proteins as well as to the mechanical blockage of the capsule itself. (4 tables, 6 references)

V. Tabone.

Orzalesi F., and Pirodda, A. **The permeability of the lens capsule to serum proteins.** *Gior. ital. oftal.* 8:191-201, May-June, 1955.

The permeability of the lens capsule was studied on material obtained from the eyes of oxen and horses; the method of electrophoresis on tissue paper was used. It appeared that while the posterior capsule was permeable to serum proteins, the anterior capsule did not behave in a similar manner. The literature on the subject is reviewed and the technique used is explained. (3 figures, 1 table, 15 references)

V. Tabone.

Orzalesi, F., Pirodda, A., and Miglior, M. **Permeability of the lens capsule to proteins positively charged.** *Gior. ital. oftal.* 8:265-271, July-Aug., 1955.

Research on material obtained from oxen and horses showed 1. that the lens capsule is permeable not only to colloids, but also to proteins (protamine, lysozyme, hystone, and globin), 2. that the permeability is not related to the electrical charge of the proteins, and 3. that the

larger the molecule the less the permeability. (1 figure, 1 reference)

V. Tabone.

Orzalesi, F., Miglior, M., and Pirodda, A. **The interaction of lens proteins with other proteins.** *Gior. ital. oftal.* 8:272-280, July-Aug., 1955.

Aqueous extracts of lenses of oxen and horses were brought into contact with different proteins. It was found that only those proteins carrying a positive electrical charge produce a turbid precipitate of the lens solution. The possible influence of these findings on the production of complicated cataract is discussed. (2 figures, 6 references)

V. Tabone.

Orzalesi, F., Miglior, M., and Pirodda, A. **The production in vitro of lens opacities by means of basic proteins.** *Gior. ital. oftal.* 8:281-288, July-Aug., 1955.

When clear lenses of oxen and horses were immersed in solutions of basic proteins, subcapsular opacities resulted. The authors had established by previous work that these opacities are formed in insoluble electrostatic proteins produced by the interaction of the electrically charged lens proteins and the positively charged proteins diffusing through the capsule. The part played by these findings in the production of complicated cataract is discussed. (3 figures, 1 reference)

V. Tabone.

Patterson, John W. **Effect of blood supply on the development of cataracts.** *Am. J. Physiol.* 180:495-497, March, 1955.

After unilateral ligation of the common carotid artery, galactose-fed rats develop cataracts on the side with the better blood supply, and hence galactose supply to the lens. This is interpreted as indicating that galactose produces cataract by acting at the level of the eye. Changing the blood supply to the eyes by unilateral common carotid ligation does not alter the develop-

ment of cataract in alloxan-induced diabetes in rats. High glucose levels may not be responsible for cataract. Cataracts may be the result of a lack of insulin. (2 figures, 20 references)

Irwin E. Gaynon.

Pisano, Elisa. **Experimental exophthalmos by thyreotrophic hormone in guinea pigs.** *Gior. ital. oftal.* 8:322-334, July-Aug., 1955.

Experiments on 14 thyroidectomised guinea pigs were carried out. Thyrotropic hormone was administered alone and with ACTH. Exophthalmos was produced by both methods, but it was most marked when both substances were used. This suggests that the use of ACTH in the treatment of malignant exophthalmos is of no value. (3 figures, 1 table, 25 references)

V. Tabone.

Remky, Hans. **Clinical methods for the quantitative and qualitative determination of the aqueous proteins.** *Arch. f. Ophth.* 156:85-89, 1954.

The author gives a short description of his own method for the quantitative determination of the amount of protein in not more than 0.015 cc. of aqueous. Qualitative determinations made use of the fact that globulins precipitate colloids and albumins protect colloids from precipitation. Recognition of changes of activity of the two groups of proteins seemed to be possible when 0.05 cc. of aqueous were used. (3 figures, 1 table)

Ernst Schmerl.

Ridge, J. W. **Sodium and chloride of the aqueous humour of normal and scorbutic guinea-pigs.** *Brit. J. Ophth.* 39:534-539, Sept., 1955.

A study made by Scholz in 1950 and again in 1953 showed that the aqueous-plasma distribution of sodium in the guinea pig differed considerably from that in other animals and also that in the scorbutic guinea pig this ratio was greatly

reduced. This work suggested that ascorbic acid is essential for the secretion of sodium into the aqueous from the plasma. Since this conclusion could have an important bearing on the whole physiology of the aqueous further experiments are planned.

It was found that the ratios of both sodium and chloride ions in the aqueous to those in the plasma were not appreciably affected by ascorbic acid depletion or saturation. These results are at variance with those of the previous investigations. (2 tables, 8 references)

Morris Kaplan.

del Rio Cabanas, J. L. **The mechanism of aqueous drainage within the eye.** Arch. Soc. oftal. hispano-am. 15:682-697, June, 1955.

A comprehensive review of the literature is presented. (9 figures)

Ray K. Daily.

Rugh, R., and Wolff, J. **Reparation of the fetal eye following radiation insult.** A.M.A. Arch. Ophth. 54:351-359, Sept., 1955.

Experiments with radiation to eyes of fetal mice revealed that although extremely radiosensitive, the retina showed remarkable powers of repair and reconstitution. (30 figures, 13 references)

G. S. Tyner.

von Sallmann, Ludwig. **Physiological chemistry of the eye.** A.M.A. Arch. Ophth. 54:605-635, Oct., 1955.

The pertinent literature for 1954 is reviewed. (188 references) G. S. Tyner.

von Sallmann, L., Tobias, C. A., Anger, H. O., Welch, C., Kimura, S. F., Munoz, C. M., and Drungis, A. **Effects of high-energy particles, X-rays, and aging on lens epithelium.** A.M.A. Arch. Ophth. 54:489-514, Oct., 1955.

Experiments were conducted which in-

dicate that the equatorial germinative epithelial cells of the lens are the most radiosensitive. The cells in the central portion of the lens are relatively radioresistant. No significant qualitative change was noted after exposure of the lens to alpha particles, deuterons, and X-radiation. The changes following exposure to radiation were not unlike those in aged rat lenses. (20 figures, 10 tables, 27 references)

G. S. Tyner.

Schirmer, R. **The influence of "Corne-cain" on the motility of the pupil.** Klin. Monatsbl. f. Augenh. 127:478, 1955.

This new local anesthetic has a slight mydriatic effect when several drops are instilled. The pupillary reactions may be reduced, but there is no effect on the accommodation nor the intraocular pressure. (4 references) Frederick C. Blodi.

Seitz, R. **The paradoxical vessel and pupil reaction.** Klin. Monatsbl. f. Augenh. 127:316-334, 1955.

These experiments are based on the clinical experience that in certain cases a field defect may become larger after an injection of a vasodilator. The author assumes that this is due to a paradoxical vasoconstriction of the retinal vessels.

The experiments were done on rabbits and the effect on the retinal vessels was studied qualitatively by the presence or absence of an intravenously injected dye. Such a paradoxical reaction could be produced 24 to 30 hours after a sympathectomy (cervical chain). The reaction could be elicited by general anesthesia or by severing the cervical spinal cord or the mid-brain. Concurrently a paradoxical pupillary reaction, i.e. a dilation of the originally miotic pupil of the sympathectomized animal occurs. (16 figures, 30 references) Frederick C. Blodi.

Shoji, I. **Effect of cortisone on experimental pseudomonas infection of the**

cornea. *Acta Soc. Ophth. Japan* **59**:1766-1769, Nov., 1955.

In rabbits, cortisone showed an accelerating action on an experimental pseudomonas infection of the cornea. (2 figures, 1 table, 16 references)

Yukihiko Mitsui.

de Simone, Silvio. **Intraocular content of vitamin C after ciliary and retrociliary diathermy.** *Rassegna ital. d'ottal.* **24**:202-209, May-June, 1955.

de Simone determined an alteration of the hemophthalmic barrier after ciliary and retrociliary diathermy, showing that in some experimental conditions there is a clear decrease in the percentage of vitamin C in the aqueous and the vitreous. This is especially true of ciliary diathermy in which alterations of the ciliary zone showed a more pronounced decrease of the vitamin. This is in accord with the view that the ascorbic acid which enters the anterior chamber arises through a process of selective secretion in the ciliary body. (7 tables, 24 references)

Eugene M. Blake.

Uesaki, H. **Influence of ultraviolet rays on vitamin B₂ content in the retinochoroidal tissue. Parts I and II.** *Acta Soc. Ophth. Japan* **59**:661-664, 1291-1298, June, Sept., 1955.

Uesaki first studied the absorption of ultraviolet rays by the transparent segments of the eye and found that only the wave longer than 320-330 m μ can reach the fundus with little absorption. Then he studied the influence of the rays on the vitamin B₂ content in the retinochoroid in vitro. He found that there was no change in the vitamin content by the rays when the tissue was exposed to the rays as a membrane. When a homogenate of the tissue was used, however, there was an increase in the vitamin after an exposure. He considers the ultraviolet rays to have an influence on the mobilization of the

vitamin. (3 tables, 8 tables, 45 references)
Yukihiko Mitsui.

Vannini, Angelo. **Coagulation of the aqueous drawn from the anterior chamber.** *Rassegna ital. d'ottal.* **24**:210-214, May-June, 1955.

In his investigation of the presence of prothrombin, the same technique was used as in the test for the utilization of prothrombin: that is, a serum was substituted for the aqueous. For the study of fibrinogen 0.1 cc. of the material was added to 0.1 cc. of the solution of the thrombin contained in 10 units, N. I. H. The time of coagulation after the aqueous was removed was then recorded. The application of this knowledge has yet to be made to the study of inflammatory conditions of the globe. (2 tables, 6 references)

Eugene M. Blake.

de Vincentiis, M. **Cholinesterase in the subretinal fluid.** *Arch. di ottal.* **59**:434-447, Sept.-Oct., 1955.

Using Ammon's method, the author confirmed the presence of cholinesterase in the subretinal fluid. Its presence does not always depend on the duration of the detachment. The enzyme is considered to be derived from the vitreous and the retina rather than from the blood. (2 figures, 1 table, 35 references) John J. Stern.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Alajmo, Arnaldo. **Aspects of amblyopia in strabismus.** *Gior. ital. oftal.* **8**:213-222, May-June, 1955.

After a preliminary discussion of amblyopia, the result of treatment in six cases of squint is described. Occlusion of the better eye was kept up for several months with good results. The importance of occlusion in all cases is stressed. (8 references)
V. Tabone.

Clerici, A., and Legorini, L. **Artificial scotoma as therapy in amblyopia with abnormal fixation.** Arch. di ottal. 59:285-316, July-Aug., 1955.

After discussing causes and diagnosis of abnormal fixation, and different methods of orthoptic therapy, the authors describe the euthyscope of Cuppers with which one can extinguish paramacular vision temporarily by creating a negative after-image of a strong light source, while macular vision is preserved. This artificial para-macular scotoma is produced 10 to 15 times and optotypes are presented to the patient to stimulate central vision. The method was used successfully in 11 cases. (2 figures, 13 references) John J. Stern.

Costarides, Jean. **The visibility of X rays.** Ann. d'ocul. 188:535-545, June, 1955.

Experiments are described which show that under conditions of dark adaptation, X radiations directed into the human eye are appreciated as light. This is not due to fluorescence of the ocular media. Nor can it be brought about by limiting the beam to the region of the occipital cortex or visual pathways. It is probable that the rods are the sensitive elements, and that the X rays are able to bleach visual purple. (12 references) John C. Locke.

Foxell, C. A. P., and Stevens, W. R. **Measurement of visual acuity.** Brit. J. Ophth. 39:513-533, Sept., 1955.

Using a black Landolt broken circle on a white ground as a test object, visual acuity was remeasured up to levels of luminance of 10,000 ft.L. with surrounds of various sizes. The values obtained by Lythgoe (1932) have thus been confirmed and extended. It is shown that acuity tends to decrease above 1,000 ft.L. and that a large surround is not necessary to high acuity. Some tests on colored Landolt broken circles are also described; difficulties of observation arose from changes in the apparent brightness of

colored test objects with size. The equipment and procedure are described in detail and relevant concepts of physiologic optics are adequately discussed. (17 figures, 1 table, 13 references)

Morris Kaplan.

La Carrere, J. Lopez. **Variations in corneal astigmatism.** Arch. Soc. oftal. hispano-am. 15:552-556, May, 1955.

La Carrere calls attention to the variations which one encounters in the ophthalmometric data of an individual case and to the variations in corneal astigmatism in different directions of gaze. The possible etiology for deviation from a stable corneal astigmatism is reviewed. The author mentions a very interesting case of a patient who had a rhythmic difference of astigmatism of one diopter, synchronous with the radial pulse. Ray K. Daily.

McFarland, R. A., and Fisher, M. B. **Alterations in dark adaptation as a function of age.** J. Gerontology 10:424-428, Oct., 1955.

There is a consistent decline in ability to see at low levels of illumination with increasing age. There is a linear correlation between the age and the final threshold level. Dark adaptation is quite limited in older subjects and may be related to decreased physiological function. Serious question of safety may be raised if the amount of available light is further reduced through the use of tinted windshields or colored glasses. (5 figures, 2 tables, 18 references) Irwin E. Gaynon.

McNeil, N. L. **Patterns of visual defects in children.** Brit. J. Ophth. 39:688-701, Nov., 1955.

The visual defects found in the children of school age and younger in a city with a population of 75,000 are described and analyzed. The results were very similar to those reported by previous investigators. The author recommends a reliable

visual test and preferably a refraction for every child early in the school year, although the latter would present a rather formidable task. Suggestions are made to avoid the lag between discovery and treatment of defective vision as well as for improving the school medical services by more timely observations. (7 figures, 8 tables, 13 references)

Lawrence L. Garner.

Poyales, A. **Spherical refraction in aphakia.** Arch. Soc. oftal. hispano-am. 15: 348-551, May, 1955.

This is an attempt to assess the value of Hirschberg's formula for the prognosis of the postoperative refraction in cases of Fukala's operation for myopia. With this objective the author analysed 187 of his own cases. Taking into consideration the entire material, the prediction of the formula was found to be fairly correct. But taking the individual cases, it was found correct in only 16 cases. From the patients' standpoint, however, the author found satisfaction with the postoperative refraction, if it was myopic, emmetropic, or hypermetropic less than two diopters. On this basis 177 cases, or 94 percent of patients were satisfied. The author concludes that Hirschberg's formula, while not absolute, is of assistance in making a prognosis of the postoperative refraction. (1 table)

Ray K. Daily.

Robinson, Edward J. **The problem of form in visual perception.** Am. J. Optometry 32:599-615, Nov., 1955.

This review may be useful as a guide to the literature on form perception. Particular attention is given to Gestalt psychology and the concepts proposed by Gibson.

Paul W. Miles.

Rougier, J., and Bongard. **How and when to prescribe contact lenses.** Ann. d'ocul. 188:672-680, July, 1955.

The authors report their examination of

300 patients for contact lenses. The prescribing of contact lenses requires a careful and complete eye examination. The wearing of the glass must be regular and progressive. A new fitting must be performed after a few months. Intolerance of the lens is generally due to tearing, daz-zling, sebaceous secretions, or anomalies of binocular vision.

John C. Locke.

Sachsenweger, R. **The Hering-Hillebrand horopter in the emmetropic and the myopic.** Arch. f. Ophth. 156:209-221, 1955.

The author studied the question whether horopter deviations of myopic people differ significantly from those of emmetropic persons. He determined the depth perception of about 380 emmetropic, 170 moderately myopic and 300 moderately hyperopic persons. Statistical evaluations of these measurements confirmed his assumption. The horopter of myopic persons showed significant differences from the horopter of emmetropic people. The conclusions seem justified (1) that different distribution of the retinal elements on the nasal and temporal sides of the fundus represent the major cause of horopter deviations in the emmetropic as well as in the myopic, (2) the spatial value of each retinal element is stable. The horopter changes produced by myopic distensions are constant, and more pronounced due to the pathologic conditions in myopia. (3 tables, 23 references)

Ernst Schmerl.

Salvado Gomez, E. **Scleral resection in the treatment of axial degenerative myopia.** Arch. Soc. oftal. hispano-am. 15: 627-636, June, 1955.

The author's material comprises 20 cases which are briefly reported. The operation consists of a lamellar resection, as practiced for retinal detachment. In cases of advanced myopia the resection is done in the region of the fundus changes,

preferably in the posterior temporal segment. The author holds that the procedure checks the distension of the sclera and other ocular tissues, prevents retinal detachment and hemorrhages due to myopia, and diminishes the myopia by several diopters. The author's indications for this operation are malignant myopia, and progressive myopia which has not as yet developed irreversible lesions. During the two-year period of observation the author found no progression in the eyes which have been operated upon. Ray K. Daily.

Sevrin, G. **Treatment of amblyopia with after-images.** Bull. Soc. belge d'opht. 109: 80-85, Feb., 1955.

The treatment of amblyopia with after-images is especially indicated in eyes with excentric fixation, in the hope of giving the fovea of the amblyopic eye correct spacial localization. A modified ophthalmoscope was used in which a special system of lenses allowed the illumination of about 30° of the retina. A much stronger light than the average was used. Two dark dots either 5° or 3° in diameter were interchangeable and protected a limited part of the retina from the glare. An enormous after-image was produced with a complimentary field of 5° to 3° in diameter. When the negative after-image appeared, a bright central field was seen with a broad grayish ring around it. The clear field corresponds to the fovea, it can be seen by the patient and may be used to regain the principal and physiologic direction of gaze. The prognosis of this treatment depends on the ease of production of the negative after-image. Among the 200 patients with extrafoveal fixation treated at the clinics at Giessen there was complete failure in only four. (1 figure)

Alice R. Deutsch.

Trincker, I., and Trincker, D. **Phenomena of contrast and integration in the for-**

mation of indistinct images. Arch. f. Ophth. 156:22-234, 1955.

The authors determined the near points of accommodation in several persons and with several methods. They emphasize the fact that near the near point indistinct images are formed not only for optical reasons but also because of phenomena of contrast and integration. (2 figures, 4 tables, 22 references)

Ernst Schmerl.

Urist, Martin J. **Eccentric fixation in amblyopia ex anopsia.** A.M.A. Arch. Ophth. 54:345-350, Sept., 1955.

In this article cases of eccentric fixation are discussed in which the "false macula" is at the angle of squint and therefore the patients show no movement with cover test. All patients had a profound amblyopia and after occlusion therapy all developed centric fixation if vision could be improved to 20/200 or more. Six months of total occlusion was considered minimal. Occlusion was maintained as long as 18 months if improvement did not occur. Best results were obtained in subjects of preschool age, but were obtained as late as 12 years of age. 20/200 vision enabled patients to continue with regular activities. Some patients lost vision in the occluded eye but concurrently gained vision in the amblyopic eye. All subjects aged four years or less obtained equal vision in the two eyes, usually 20/20 or 20/30. (2 figures, 5 tables, 11 references)

G. S. Tyner.

Walton, Howard N. **Visual and reading improvement in industry.** Am. J. Optometry 32:563-576, Nov., 1955.

The average college student in simple reading must make and break fusion eight times per 10 word line. The speed of fusion is therefore very important in rapid reading. Fusion precision depends on the extent of Panum's fusional areas, which in turn can be doubled by training. Industrial

training with the tachistoscope has resulted in reading rate gains of 20 percent with better comprehension. It works by presenting a word in so brief a time that it must be interpreted as a unit and with cones farther from fixation. Results of training of 56 bank employees are discussed.

Paul W. Miles.

5

DIAGNOSIS AND THERAPY

Ainslie, D. **Treatment of superficial ocular infection with a polymyxin-bacitracin ointment (polyfax).** *Brit. J. Ophthalm.* 39:557-562, Sept., 1955.

Since it is difficult to make bacteriological studies of every case of superficial eye infection, it becomes important to employ a bacteriocidal agent which will react with the widest range of bacteria. In this study an ointment containing 400 units of bacitracin and 10,000 units of polymyxin "B" per gram was used in laboratory studies as well as in clinical trials. In experimental studies it was found to be effective against gram-positive and gram-negative organisms as well as against *Ps. pyocyaneus*. In the clinic it was found to be very effective in the treatment of blepharitis and corneal ulceration as well as being a prophylactic against infection after corneal abrasion. The medication is neither irritating nor toxic, and causes no sensitivity reactions. (3 figures, 9 references)

Morris Kaplan.

Albrecht, H., and Berneaud-Kötz, G. **Precision of the commercially available tonometers.** *Klin. Monatsbl. f. Augenh.* 127:515-528, 1955.

The authors examined eight entirely new German tonometers. All were sold with the guarantee that they correspond to the standardization factors of the Committee on Standardization of Tonometers of the American Academy of Ophthalmology and Otolaryngology. They were

examined according to these standards and none of these new tonometers was found to meet all these criteria. The authors urgently advise the standardization of German tonometers and believe that the criteria could be even more stringent. (5 figures, 3 tables, 47 references)

Frederick C. Blodi.

Boberg-Ans, Jørn. **Experience in clinical examination of corneal sensitivity. Corneal sensitivity and the naso-lacrimal reflex after retrobulbar anaesthesia.** *Brit. J. Ophthalm.* 39:705-726, Dec., 1955.

A new method of examining corneal sensitivity is suggested to obviate the present inexact method in which wisps of cotton are used. The author modifies the von Frey method by substituting an adjustable nylon thread in a special holder and feels that this method is clinically reliable. The test is of value in certain types of neurologic disturbance. The test is used to show the value of adding hyaluronidase to the retrobulbar injection by observing the beneficial effects insofar as corneal anesthesia is concerned. (28 figures, 17 references)

Lawrence L. Garner.

Buerger, M. **Ageing and disease.** *Klin. Monatsbl. f. Augenh.* 127:257-284, 1955.

This is a review article on some geriatric problems. Tissues with poor vascularization and low metabolism are better suited for evaluating senile changes. These tissues dispose of their metabolites by diffusion and usually show pronounced morphologic changes with age, such as the senile arcus in the cornea, the cataract in the lens or the calcification of cartilage. All these tissues lose water and gain calcium or cholesterol. At the same time the nitrogen content decreases as substances are deposited which contain less nitrogen, for instance chondroitin sulfuric acid in the walls of big vessels.

While the arterial pressure rises with

age the venous pressure falls and this may account for the decreasing exophthalmometer readings in senescence. In a similar way there is a decrease in capillary resistance which may be of influence in diabetic retinopathy. Even the ganglion cells of the brain undergo chemical and morphological changes with age. (30 figures, 8 tables, 34 references)

Frederick C. Blodi.

Delogu, A. **The value of the Middlebrook-Dubos hemoagglutination reaction in ophthalmology.** *Boll. d'ocul.* **34**:484-497, Aug., 1955.

Considerable lack of agreement exists among ophthalmologists as to the frequency of tuberculous infection of the eye. Unfortunately the diagnosis of ocular tuberculosis frequently is tenuously based on the history and clinical findings. In 1948 Middlebrook and Dubos reported that a hemoagglutination reaction could be elicited from the serum of tuberculous patients. From his studies of this reaction in patients with ocular disease the author concludes that the Middlebrook-Dubos reaction may be of value in the diagnosis of ocular tuberculosis. (2 tables, 30 references)

William C. Caccamise.

Duke-Elder, S., and Goldsmith, A. J. B. **Cortisone and corticotrophin in ophthalmology.** *Practitioner* **175**:577-582, Nov., 1955.

The authors point out the great value of these drugs and also emphasize the dangers of misuse. The corticosteroids all have similar actions. They block the exudative phase of inflammation and inhibit fibroplastic proliferation in the process of repair. The effect is the same whether the cause of the inflammation be bacterial infection, anaphylaxis, allergy, or trauma. The drug inhibits the response of mesenchymal tissue to an irritant; it does not

influence the cause of the inflammation. When the hormone is withdrawn, the disease process may resume its course as before, or even with increased vigor. Cortisone is not effective in the removal of fibrous tissue or in the repair of structural damage. The essential role of cortisone in most infective processes of the eye is the control of excessive inflammatory response. In the eye it is particularly important to limit exudation and fibroplastic proliferation while an etiologic cure is being achieved by other agents. The advantages and dangers of the use of the corticosteroids are most clearly exemplified in the case of tuberculosis. When the condition is allergic or exudative, cortisone may well be of temporary benefit, but if a caseating lesion be present or the eye be invaded by tubercle bacilli, the use of these hormones may have disastrous consequences. The eye may remain white but there will be uninhibited multiplication of the bacilli. This has been shown to be true experimentally and clinically in bacterial choroiditis where the administration of corticosteroids has been followed by the conversion of a localized lesion to a widespread diffuse infection spreading over the entire fundus.

F. H. Haessler.

D'Ermo, F., and Guzzinati, G. C. **Anti-histaminics and the eye.** *Boll. d'ocul.* **34**:449-459, Aug., 1955.

The authors studied the effects of a systemically and locally administered antihistaminic (Antistine Ciba) on Evans angioscotomy and Goldmann's artificial scotoma. Systemic administration produced a narrowing of the scotoma, attributed by the author to vasoconstriction. Conjunctival instillation produced no change. Subcutaneous injection of histamine resulted in an enlargement of the scotoma, attributed to vasodilatation. (6 figures, 27 references)

William C. Caccamise.

Giggelberger, Hans. **X-ray diagnosis of the skull.** *Klin. Monatsbl. f. Augenh.* 127:390-399, 1955.

A few cases are described in which the radiologic diagnosis was of great importance. In a 29-year-old woman with headache and loss of vision (central and peripheral) X-ray films showed the typical signs of hyperostosis of a suprasellar meningioma.

A 33-year-old woman had marked asymmetry of the face, loss of vision on the hypoplastic side and headache for eight years. X-ray study revealed an enlargement of one optic canal and numerous osseous anomalies. The skin changes also spoke for von Recklinghausen's disease.

A 58-year-old man came because of epiphora on one side. The dacryocystogram showed a tumor of the antrum invading the nose and the orbit.

The last patient was a 46-year-old woman with headache and unilateral palsy of the third nerve. The X-ray picture of the skull showed an erosion of the sella. (14 figures, 5 references)

Frederick C. Blodi.

Hamada, K. **A study on the blood pressure of the ciliary vein. I.** *Acta Soc. Ophth. Japan* 59:1701-1704, Nov., 1955.

This is an introduction of a new compression apparatus for a measurement of ciliary vein pressure. Hamada employed a small ammeter. A rod is fixed on the needle of the ammeter for compression of the vein. A minimum compression can be done with this apparatus. By changing the intensity of the electric current passing through the ammeter, he changes the degree of compression. With this apparatus the measurement can be done more easily than with the pressure cushion method by Seidel. According to the author's measurement in 50 normal men, the pressure of the ciliary vein is in the

range of 5.8 to 17.9 mm. Hg. (2 figures, 2 tables, 14 references)

Yukihiko Mitsui.

Krannig, H., and Koehler, W. **The antistreptolysin titer in ophthalmology.** *Klin. Monatsbl. f. Augenh.* 127:565-576, 1955.

112 patients were examined. The titer was high in 11 out of 43 patients with acute iritis and in 4 out of 35 patients with chronic uveitis. An increased titer was also found in patients with neuritis, retinitis, keratitis and scleritis. The importance of a titer curve for recognition of the organism that caused an ophthalmic inflammation is stressed. (4 illustrations, 2 tables, 15 references)

Frederick C. Blodi.

Kruemmel, H. **A lens supporter for the ophthalmoscope.** *Klin. Monatsbl. f. Augenh.* 127:601, 1955.

A detachable supporter for the indirect ophthalmoscope or the non-illuminating retinoscope is described. It serves for the optical correction of the presbyopic or ametropic physician. (2 figures)

Frederick C. Blodi.

Offret, G. and Saraux, H. **Bacteriologic study of the aqueous humor.** *Arch. d'opht.* 15:573-596, 1955.

The authors have made 126 anterior chamber punctures in 113 different patients with a variety of conditions including hypopyon ulcer, corneal diseases, intraocular foreign bodies, and a number of types of uveitis, including heterochromic cyclitis. Their report opens with a historical review of aqueous examinations. They then describe their techniques of exploration of the aqueous which depended on the use of a capillary tube designed by Magitot and a trochar designed by Amsler. The aqueous was subjected to cell count, measurement of protein, and bacteriologic study.

The results of these studies are reported in considerable detail. For example, 30 cases of uveitis are described which the authors believed to be of infectious origin because of association with a known focal infection. In six instances they cultivated bacteria which they believed to be from the aqueous, and in the aqueous from eight patients they saw bacteria in cells. In 11 cases of uveitis without associated focal infection they were unable to cultivate bacteria or to see bacteria in cells from the aqueous. They found bacteria (staphylococci) in three of six cases of uveitis that followed cataract extraction. The authors speculate on the significance of these findings and conclude that the bacteria found were probably significant. A second part of this study is to follow in the next issue. (8 tables)

P. Thygeson.

Offret, G., and Saraux, H. **Bacteriologic study of the human aqueous.** Presse Med. 63:1513-1515, Nov. 9, 1955.

Simple puncture of the anterior chamber with a small needle attached to a capillary tube secures five or six drops of aqueous. A drop is used respectively for cell study, measurement of albumin and culture, and two drops are centrifuged for a Giemsa stain of the sediment. Contrary to the current view that hypopyon keratitis represents a sterile reaction in the aqueous, positive cultures are the rule. In uveitis from focal infection positive cultures are also obtained, though not in true rheumatoid affections. Cultures have usually been positive in foreign body penetration and traumatic erosion of the cornea; negative in superficial punctate keratitis, interstitial keratitis, suspected tuberculosis, and chemical burns of the cornea. In heterochromic uveitis positive cultures are surprisingly frequent. (6 figures)

James E. Lebensohn.

Quintieri, C. **Additional observations**

on the use of Mintacol. Boll. d'ocul. 34:478-483, Aug., 1955.

The author has used Mintacol in a large number of patients. He concludes that it is a miotic with a wide range of use in ophthalmology. The article treats specifically the author's use of this drug in glaucoma, cataract surgery, and keratoplasty. (7 references)

William C. Caccamise.

Raimondo, N. **Some clinical applications of hyaluronidase in ophthalmology.** Boll. d'ocul. 34:433-442, July, 1955.

The author discusses the effect of subconjunctivally administered hyaluronidase on 1. both spontaneous and traumatic hyphemas, 2. both spontaneous and traumatic vitreous hemorrhages, 3. the clearing of corneal leucomas, 4. the diffusion of medicaments into the interior of the eye, and 5. on ocular tension. (31 references)

William C. Caccamise.

Stallard, H. B. **Modified ptosis spatula.** Brit. J. Ophth. 39:573-574, Sept., 1955.

The author describes a ptosis spatula which differs from the usual one in being much more curved to protect the cornea and in being perforated along its border so that the stretched lid can be sutured to keep it expanded as an aid in levator surgery. (2 figures, 3 illustrations)

Morris Kaplan.

6

OCULAR MOTILITY

Börner, R. **Oculomotor disturbances in endocrine exophthalmus.** Klin. Monatsbl. f. Augenh. 127:403-411, 1955.

Of 10 patients with endocrine exophthalmus 9 had an increased BMR and the tenth patient had a BMR of -2 . In all, at least one superior rectus muscle was paretic. In half of the patients both eyes were involved. Five patients had had a thyroidectomy, but two of them had di-

plopia before the operation. In three patients a temporary rise in tension occurred in the involved eye. (6 figures, 16 references) Frederick C. Blodi.

Lloyd, J. P. F. **Left paralytic convergent squint.** *Brit. J. Ophthalm.* 39:572, Sept., 1955.

A 72-year-old woman had paresis of the left external rectus muscle for 20 years and despite her age requested a cosmetic correction. After surgery, in which strips of the superior and inferior rectus muscles were attached to the insertion of the paralyzed rectus muscle and a recession of the internal rectus of 6 mm. was done, convalescence was uneventful. Full normal movement returned and vision was 6/5 with almost complete freedom from diplopia. Morris Kaplan.

Schenk, H. **Artificial paresis of extraocular muscles.** *Klin. Monatsbl. f. Augenh.* 127:592-595, 1955.

Previously, (*Kl. Mbl. Augenh.* 127:306) the use of the longlasting local anesthetic rhaetocain for a temporary paralysis of an ocular muscle after a strabismus operation was described. This report is here followed by animal experiments. The drug was injected into the gluteal muscles of rabbits. It disappeared after 12 hours, but histologic changes persisted for more than 15 days. (3 figures, 1 reference)

Frederick C. Blodi.

7

CONJUNCTIVA, CORNEA, SCLERA

Agarwal, L. P., and Malik, S. R. K. **Tetracycline in trachoma.** *Brit. J. Ophthalm.* 39:759-761, Dec., 1955.

Using oral tetracycline as well as local therapy results in the disappearance of the trachoma virus in about 40 percent of the patients as shown by the absence of inclusion bodies from the smears. The drug is rather quick-acting since this re-

sult was noted in about three weeks. The drug seemed to be particularly effective in trachomatous keratitis and its regressive effect upon pannus is noted. The drug is not as effective as the sulfonamides but is probably of value as an adjunct to the latter or as a substitute in sulfonamide-resistant cases. (1 table, 7 references)

Lawrence L. Garner.

Aguilar Bartolome, Jose M. **Calcareous concretions of the conjunctiva.** *Arch. Soc. oftal. hispano-am.* 14:1429-1450, Dec., 1954.

In this exhaustive monograph the literature of all its phases is covered. It is pointed out that the majority of concretions diagnosed as calcareous do not contain calcium; they consist mostly of mucus and epithelial cells. Calcium deposit is never a primary process but always secondary to hyaline or amyloid degeneration, necrosis and caseation. Calcium infiltration is a type of burial of dead or foreign cells. The author also differentiates between true and false calcinosis. True calcinosis is encountered in so-called conjunctivitis petrificans, spring catarrh, trachoma, tuberculosis of the conjunctiva, syphilis, erysipelas, neoplasms, chemical injuries, and in glandular deposits in hypercalcemia. As false calcinosis are mentioned, lithiasis nodules of the Meibomian glands, dacryoliths, calcification of the conjunctiva and sclera in atrophic globes, and intentionally introduced calcium particles by malingerers. The histopathology, etiology, classification and treatment are reviewed. Among the therapeutic procedures mentioned, in addition to attacks on the etiologic factor, are heat, Grant's method in which Edta is used, constitutional measures, and excision. (43 references) Ray K. Daily.

Alimuddin, M. **Treatment of vernal conjunctivitis.** *Brit. J. Ophthalm.* 39:540-544, Sept., 1955.

In this study, the results of treatment of 1,050 cases of this disease are evaluated. The results as a whole have been disappointing and no satisfactory therapeusis was evolved. The greatest benefit was obtained by removing the patient to a different climate, particularly a change from the desert areas to the high hill areas; this alleviated the symptoms but did not prevent recurrence. The usual treatment of allergies and particularly the destruction of intestinal parasites brought some relief. Diet was less important and irradiation, here by X-ray, brought no appreciable relief. The instillation of cortisone in 1-percent solution or ointment brought about the most satisfactory amelioration of symptoms. (6 tables, 15 references)

Morris Kaplan.

Dark, A. J. **Inclusion bodies in trachoma.** *Brit. J. Ophth.* 39:751-758, Dec., 1955.

The author uses histochemical methods to demonstrate the presence of nucleic acids and carbohydrate in the inclusion bodies. By this method the initial and elementary bodies are shown to contain deoxyribonucleic acid, while the "plastin" substance of Prowazek is identified as ribonucleic acid. Poleff's method of staining is evaluated and found not suitable for identifying the Halberstaedter-Prowazek inclusion body, while the classical Giemsa stain is still found to be the best. The author suggests that thin smears of the palpebral conjunctival epithelial cells be used, instead of scrapings, in the diagnosis of trachoma. (9 figures, 15 references)

Lawrence L. Garner.

Fanta, H. **Superficial keratitis with temporary loss of epithelium.** *Klin. Monatsbl. f. Augenh.* 172:431-437, 1955.

Five patients with an unusual corneal disease were observed. It started with a conjunctival irritation but soon the cornea became involved. The entire epithelium

may be shed but there are no opacities or infiltrates and the epithelium regenerates after a few days. The patients suffer from a severe pain for a long time. The corneal sensitivity is reduced. The condition improves with antibiotic ointments and binocular bandage. In the differential diagnosis, epidemic keratoconjunctivitis, herpes, neuroparalytic keratopathy and punctate keratitis was considered. (4 references)

Frederick C. Blodi.

Heydenreich, A. **Corneal vascularization in animal experiments.** *Klin. Monatsbl. f. Augenh.* 127:465-471, 1955.

This is a summary of animal experiments to produce corneal vascularization. A stromal edema is a prerequisite of corneal vascularization. A central lesion will only produce a vascularization if the surrounding edema reaches the limbus. A limbal or peripheral lesion will more frequently cause vascularization as the adjacent edema has a better chance to reach the limbus. The corneal lesion was either a simple abrasion or a coagulation. In other instances a chemical irritant was added to the abrasion. Cortisone did not influence the edema nor the vascularization. Substances with hygroscopic properties (glycerine, 35 percent detrose) decreased the edema but inhibited the reparation and larger scars resulted. (2 figures, 12 references)

Frederick C. Blodi.

Hofmann, H. **Epidemic keratoconjunctivitis in Styria 1952-1954.** *Klin. Monatsbl. f. Augenh.* 127:438-465, 1955.

In this epidemic in one Austrian state 200 cases were observed. The clinical picture is described in detail. The early edema of the semilunar folds and the caruncle are emphasized. Pseudomembranes are occasionally seen. Follicles appear soon and the regional lymph glands were swollen in 18 percent of the

cases. The disease was bilateral in 90 percent of the patients. The inflammation also occurs in a milder form in children. In 99 percent of the patients there are corneal lesions, the first traces of which appear on the fourth or fifth day. The local application of convalescent serum and potassium permanganate together with nonspecific fever therapy proved most successful. In the differential diagnosis nummular keratitis and superficial punctate keratitis are especially considered. Intracytoplasmic inclusion bodies could be found in numerous smears and scrapings. (9 illustrations, 147 references)

Frederick C. Blodi.

Leigh, A. G. **Treatment of gross corneal opacification by lamellar and annular lamellar keratoplasty.** *Brit. J. Ophthalmol.* 39:641-646, Nov. 1955.

The author presents an interesting modification of keratoplasty, designed particularly to be used when there is extensive opacification through all layers of the cornea. A simple penetrating graft frequently takes on the characteristics of the tissue into which it is placed and the author presents a technique designed to prevent this spread of degeneration. Initially a 6 mm. lamellar graft is placed into the recipient cornea and held by indirect sutures. Within six to eight months sensitivity is noted in the graft, and if successful, it will be clear and free from vascularization. Some fine vascularization may be noted beneath the graft adjacent to the recipient cornea, but this is no contraindication to the next stage of annular grafting. At this time a 10 mm. and 7 mm. trephine are used to outline a ring of tissue from the donor cornea which is removed to a thickness of about 5 mm. This is now centered on the recipient cornea, after removal of a similar annulus. After this stage has gone through complete healing, the patient is finally ready for his final, 5 mm. penetrating

donor graft through the initial site. This final perforating grafting must not be performed until both previous lamellar grafts are relatively clear. If they are not clear they must be renewed. The author reports three cases showing good results in two years of observation. This technique seems to be effective in preventing the vascularization which is so detrimental in this type of surgery. (14 figures)

Lawrence L. Garner.

Ormsby, H. L. **An interim report on ocular diseases due to APC viruses in Ontario.** *Canad. J. Pub. Health* 46:500-505, Dec., 1955.

Epidemics of viral conjunctivitis with corneal opacities occurred in Ontario in 1951 and in 1955. Sera from four patients with EKC in the Windsor epidemic of 1951, and from two patients with EKC in Toronto in November, 1954, had neutralizing antibodies to the type 8 APC (Trimborn) virus of Jawets. From November, 1954, until June 15, 1955, 20 adult patients with viral conjunctivitis were studied. Half of these patients developed minor corneal opacities, and from eye washings from seven, virus was isolated in tissue cultures of HeLa cells or monkey-kidney. Three of these strains of virus were sent to the virus laboratories of the National Institutes of Health and were found to belong to the type 3 APC group of viruses. A widespread epidemic of pharyngeal-conjunctival fever in children and adults occurred in Ontario in the summer of 1955. This was transmitted primarily in swimming pools, and secondarily by direct contact. (3 tables, 18 references)

Irwin E. Gaynon.

Radaban Fernandez, Pedro. **Double binocular pterygia.** *Arch. Soc. oftal. hispano-am.* 14:1423-1428, Dec., 1954.

This is a report of bilateral double pterygia, the only case the author encountered among 742 cases of pterygium.

The etiology of pterygium is reviewed. Practicing in one of the most arid regions of Spain, the author believes that chronic inflammation of the conjunctiva and lacrimal passages, glare, wind and dust are etiologic factors. (2 figures, 12 references)
Ray K. Daily.

Shah, M. A., and Shah, M. **Essential shrinkage of the conjunctiva in epidermolysis bullosa hereditaria.** *Brit. J. Ophth.* 39:667-672, Nov., 1955.

A study is presented of a case of essential shrinkage of conjunctiva in which the findings were compatible with epidermolysis bullosa hereditaria. The hereditary nature of the affection, the skin, and conjunctival lesions, and the histopathological findings of the skin suggest the diagnosis. It will be noted that there is subepidermal slit formation in contradistinction to intraepidermal slits as in pemphigus. (5 figures, 7 references)

Lawrence L. Garner.

Walser, E. **Experience with perforating keratoplastic surgery based upon 71 transplantations.** *Arch. f. Ophth.* 156:127-153, 1955.

Sixty-two patients with 71 transplantations were observed for periods of from one to eight years. Most of the patients were 20 to 50 years old, two thirds of them were males. Surgery was performed in 12 cases of corneal opacity due to trauma, in 44 of opacity following infections or other diseases, and in 15 due to degenerative changes. Prognosis seemed to be best in avascular corneas, for example in congenital dystrophies, keratoconus and circumscribed leucomas. Good anatomic results were obtained in about 80 percent of the cases, good functional results in about 50 percent. The material used for the transplantation in 29 cases came from eyes enucleated for tumor, in 42 from corpses. Possible allergic reactions of the host were prevented by injec-

tions of calcium, cortisone and other substances. (2 tables, 4 references)
Ernst Schmerl.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Bennet, George. **Uveitis. A clinical and statistical survey.** *Brit. J. Ophth.* 39:727-742, Dec., 1955.

Faced by our ignorance of the basic causes of much uveitis, the author devised a classification based on three positive associations which may or may not possess etiologic significance and does avoid the various analogies and presumptions inherent in other schemata. He has applied it to 322 cases of primary uveitis which he has studied; 66 (20 percent) were classified as Group A—Collagenous Disease, 127 (38 percent) Group B—Local Virus Infection, 15 (4.5 percent) Group C—Systemic Disease—Granulomatous Uveitis, and 124 (37.5 percent) Group D—Unclassified. Investigational analysis justifies certain beliefs. It confirms the validity of the nosology described and suggests a basis for the organismal etiology of uveitis. It indicates the worthlessness of much expensive clinical investigation of patients and of their therapy and urges that greater attention be paid to old-fashioned history taking and clinical study of the patient as a whole. (1 figure, 18 tables, 89 references)

Lawrence L. Garner.

Ikui, H., and Furuyoshi, Y. **Experimental studies on the pathogenesis of sympathetic ophthalmia, Harada and Vogt-Koyanagi syndrome.** *Acta Soc. Ophth. Japan* 59:1481-1498 Sept., 1955.

This is an attempt to isolate viral agents from sympathetic ophthalmia and like conditions. The original material for virus isolation were the uvea of removed eyes and the vitreous or subretinal fluid

obtained by a puncture. Aqueous humor and spinal fluid were also employed in some cases. The first inoculation was done in mouse brain. After 25 successive blind passages, there appeared no "take" in the animal. An addition of cortisone did not favor the isolation. Then the authors employed the chorioallantoic membrane of chick-embryo. The result was also negative. Finally, they inoculated the material from 17 patients into the vitreous of rabbits. The material from 13 of the 17 patients caused an acute uveitis in the rabbit eye. The ultrafiltrate through Seitz-EK of the material was also able to produce the same uveitis in some cases (3 of the 8 examined cases). The uveitis was brought about one to two weeks after the inoculation in each case and it lasted up to three weeks. The uveitis was not transmitted to the second eye spontaneously. However, a sub-transfer was possible by inoculation in some cases. Histologically, the uveitis thus produced had certain similarities to that seen in man. (2 figures, 10 tables, 27 references)

Yukihiko Mitsui.

Mehta, K. H. **Congenital toxoplasmosis.** *Brit. J. Ophth.* 39:569-571, Sept., 1955.

Congenital toxoplasmosis in two children is described; each had diminished vision due to large patches of quiescent chorioretinitis. Each had a positive toxoplasma antibody test and each had a younger sibling who was unaffected. It is probable that the mother transmitted the infestation to the child and then developed antibodies which prevented further development of the disease in herself. (6 figures, 4 references)

Morris Kaplan.

Pagliarani, N. **Value of endocular biopsy to ascertain the nature of melanomas of the choroid.** *Gior. ital. oftal.* 8:229-241, May-June, 1955.

The literature of the different proced-

ures is reviewed, and emphasis laid on the difficulties of the procedures. Five cases in which this investigation was carried out are described in detail, and the limitations and the value of the different methods employed are described. This method of investigation should be resorted to only when no other diagnostic help is available. (2 figures, 28 references)

V. Tabone.

Ryan, R. W., Hart, W. M., Culligan, J. J., Gunkel, R. D., Jacobs, L., and Cook, M. K. **Diagnosis and treatment of toxoplasmic uveitis.** *Tr. Am. Acad. Ophth.* 58:867-884, Nov., 1954.

The authors present a preliminary report indicating that toxoplasma infection is an important factor in adult chorioretinitis. They discuss treatment with Daraprim and sulfa drugs, mainly sulfadiazine. (4 photomicrographs, 9 tables)

Theodore M. Shapira.

Scullica, Francesco. **Traumatic epithelial cyst of the iris.** *Rassegna ital. d'ottal.* 24:251-268, July-Aug., 1955.

Twenty-two years after a penetrating wound of the left cornea by scissors, the patient presented himself with a cyst of the iris. This arose at the limbus in the lower quadrant. There was also a pigmented patch on the adjacent sclera. Focal illumination showed a translucent cyst with a velvety surface and pigment granules. The cyst was composed of three lobes. There was no inflammation of the eye, the lens was clear and the fundus appeared normal. Surgery was advised but refused. Five months later the eye showed pericorneal congestion and some enlargement of the cyst. These changes increased and led to eventual operation for removal of the cyst. Histologically the cyst consisted of three layers, an external, a basal and an epithelial layer. Cataract developed and was later extracted. The

literature on traumatic cysts of the iris is reviewed. (5 figures, 56 references)

Eugene M. Blake.

Smith, C., and Ashton, N. **Studies on the aetiological problem of uveitis.** Brit. J. Ophth. 39:545-556, Sept., 1955.

Two hundred patients were studied and classified as to age, sex, and clinical category and it immediately became obvious that there was a significantly greater incidence of anterior uveitis in females and an earlier onset of posterior uveitis in males. There were no cases of positive Wassermann or Kahn reactions. The gonococcal complement-fixation test was positive in only two cases and in neither was a history of venereal infection obtained. The Middlebrook-Dubos and Mantoux tests failed to indicate any relationship to tuberculosis. Complete blood counts revealed no significant irregularities and serum agglutination tests for Brucella indicated no causal relationship. Toxoplasma tests were positive in a high percentage and although high titer levels are not diagnostic in individual patients, it is difficult to believe that this association is not etiologically significant. It was found that in anterior uveitis there was much more than an ordinary ratio of positives in anti-streptolysin assays, which suggests a probable association between previous streptococcal infection and anterior uveitis. (5 tables, 38 references)

Morris Kaplan.

9

GLAUCOMA AND OCULAR TENSION

Agarwal, L. P., Sharma, K., and Malik, R. K. **Diamox therapy in flat chamber.** Brit. J. Ophth. 39:664-666, Nov., 1955.

Of 45 cases of postoperative flat chamber which are reviewed, 25 occurred after cataract extraction, 10 after trephining and 10 after iridencleisis. Patients in

whom the chamber failed to reform by the fifth postoperative day were given diamox orally for a maximum of seven days. The dosage was 250 mg. morning and evening. In 23 eyes the disturbance was complicated by choroidal detachment; this observation emphasizes the importance of adequate fundus examination. The chamber was restored in 40 of the 45 eyes. (1 table, 2 references)

Lawrence L. Garner.

van Beuningen, Ernst G. A. **Slitlamp gonioscopy as diagnostic help in primary chronic glaucoma.** Arch. f. Ophth. 156: 35-67, 1954.

The author developed his own methods and special instruments in order to study 1. normal and glaucomatous eyes with respect to pigmentation of Schlemm's canal, density and color of the corneoscleral trabeculum, and color of the anterior surface of the ciliary body, 2. spatial relations and depth of the angle of the anterior chamber. 223 normal eyes and 439 eyes with chronic simple glaucoma were examined. Of the normal eyes 44 percent showed pigmentation of the area of Schlemm's canal and in glaucomatous eyes pigmentation was found in 68 percent. Age did not seem to play a significant role in these findings but increase in tension was associated with an increase in pigmentation. A less pronounced correlation was found between density of the trabeculum and increase in ocular tension. Increased density in glaucomatous eyes in comparison with normal eyes seemed already to exist in younger years. It did not seem to be correlated to the aging process. Loss of color of the anterior surface of the ciliary body occurred in glaucomatous eyes as often as in normal ones. In both groups a positive correlation existed between age and decoloration. The angle of the anterior chamber was found to become narrow with age in glaucomatous eyes and not in normal

ones. (8 figures, 25 tables, 34 references)
Ernst Schmerl.

Blaxter, P. L. **Symptoms of congestive (closed-angle) glaucoma occurring in eyes with a wide chamber angle.** *Brit. J. Ophth.* 39:673-680, Nov., 1955.

The author presents three cases of glaucoma simplex in which the presenting symptoms of halos and blurred vision suggest congestive glaucoma. It is rare for an open-angle type of glaucoma to present such symptoms and this report brings out the importance of a thorough examination in arriving at a proper diagnosis. Gonioscopy is essential in determining the type of chamber angle and can eliminate the possibility of performing an iridectomy where a filtering operation is indicated. (13 references)

Lawrence L. Garner.

Boles-Caronini, B. **Principles, technique, and practicability of tonography.** *Boll. d'ocul.* 34:403-432, July, 1955.

The author very capably and thoroughly covers the subject of tonography. (3 figures, 4 graphs, 3 tables, 52 references) William C. Caccahise.

Comberg, W. **Paraglaucoma—posterior and anterior.** *Klin. Monatsbl. f. Augenh.* 127:514-515, 1955.

The author designates as anterior paraglaucoma eyes with low tension glaucoma. Such eyes, on the other hand, which appear to have an increased intraocular pressure without any other signs of glaucoma are called posterior paraglaucoma. (Resistance to outflow or scleral rigidity are not discussed.) Frederick C. Blodi.

Cristini, G., and Pagliarana, N. **Slit-lamp study of the aqueous veins in simple glaucoma during the amyl nitrite test.** *Brit. J. Ophth.* 39:685-687, Nov., 1955.

The authors find that blood appears in the aqueous veins in normal or glaucomatous eyes rather constantly when amyl

nitrite is given by inhalation. This phenomenon has been previously reported as occurring with the use of any vasodilatory drug. Since aqueous veins are difficult to see, in patients with tension over 35 mm. Hg, this test is applicable only to patients who have low elevations of tension. A concurrent transitory drop in the ocular tension which was noted is not explained. (8 references) Lawrence L. Garner.

Drance, S. M. **Glaucoma treated with diamox. Preliminary report of 20 cases.** *Brit. J. Ophth.* 39:659-663, Nov., 1955.

No intravenous injection of diamox had been used and all results are based on the oral administration of the drug with or without the use of miotics. The best results were noted in the secondary and congestive types of glaucoma and the poorest in the chronic, open-angle form of glaucoma. An initial oral dosage of 500 mg. at 6-hour intervals was followed by a reduction in dosage as the tension fell; 30 grains of sodium bicarbonate was given with the diamox and a minimal dose of 125 mg. of diamox seemed most effective when given two or three times a day. The author points out that the maintenance dose must be worked out by trial and error. All patients complained of tingling in the extremities, even with minimal dosage, but this is no contraindication to this form of therapy. (2 tables, 2 references) Lawrence L. Garner.

Friede, Reinhard. **A keyhole-shaped trephine as a glaucoma operation.** *Klin. Monatsbl. f. Augenh.* 127:536-538, 1955.

In order to enlarge the area of fistulation a trephine opening is enlarged with a punch to form a keyhole-shaped opening. (6 figures) Frederick C. Blodi.

Gloster, J., and Perkins, E. S. **Effect of a carbonic anhydrase inhibitor (diamox) on intra-ocular pressure of rabbits and**

cats. Brit. J. Ophthalm. 39:647-658, Nov., 1955.

The results noted here corroborate the findings of Becker, Grant and Trotter insofar as they reveal a rapid drop in intraocular pressure when diamox is given intravenously. A transient rise in pressure is noted at times in some animals which is soon followed by a drop, and this initial response is believed to be due to a temporary vasodilator action of the sodium diamox solution. The local or subconjunctival use of diamox was without effect, and so was the injection into the anterior chamber or the carotid artery. (9 figures, 4 tables, 9 references)

Lawrence L. Garner.

Kleinert, Heinz. **Periodic contractions of the anterior ciliary arteries and ocular tension.** Arch. f. Ophthalm. 156:68-78, 1954.

The author took pictures of ten normal and ten glaucomatous eyes several times a day. He also determined the ocular tension at the time the pictures were taken. When the arteries showed contractions an increase in tension was observed. The author feels that the narrowing of the bloodvessels produced an angioneurotic scleral edema and the increase in tension. (4 figures, 4 references) Ernst Schmerl.

Niesel, P. **The effect of rapid changes of atmospheric pressure upon ocular tension.** Arch. f. Ophthalm. 156:79-84, 1954.

When rabbits and men were exposed for short periods to an air pressure corresponding to an altitude of 7,000 to 8,000 meters, a short increase in tension up to about 7 mm. Hg was observed. The changes in tension were not exactly paralleled by changes in general blood pressure. However, with the higher ocular pressure the blood volume of the head seemed to increase. (3 figures, 15 references) Ernst Schmerl.

Sanchez Salorio, M., and Barcia Salorio,

J. L. **A contribution to the study of the nervous regulation of ocular tension.** Arch. Soc. oftal. hispano-am. 14:1373-1408, Dec., 1954.

This is a report of an investigation on the effect of electric stimulation of the brain. Electric shock was produced by an alternating current of 75 volts. The orbicularis was sectioned, and the ocular tension measured in the tonic and clonic stage of the convulsions. The effect of stimulating the separate parts of the brain was studied by two methods. In one a solenoid of copper was imbedded in the area to be investigated, and the experiment made after the animal recovered from the surgical procedure. The tension was also taken after direct stimulation of the various areas with an alternating current through a monopolar electrode applied to the exposed cerebrum. In some cases a bipolar faradic stimulus was also used. The details of these experiments are described and illustrated in detail, and the data recorded graphically. The results show that massive excitation of the brain produced a marked transitory rise in ocular tension, which is not affected by the exclusion of muscular contraction, but is eliminated by preliminary blocking of the hypothalamus by drugs. This elevation in tension is followed by a slow and moderate fall, from which the tension slowly returns to normal. The excitation of the frontal, parietal, temporal and occipital areas produced no modifications in the ocular tension. The excitation of the olfactory bulb and the cingulum produced a synergic excitation of the basal nuclei of the diencephalus and of the amygdaline nucleus. The direct excitation of these nuclei also produced a moderate fall in ocular tension. (29 figures)

Ray K. Daily.

Serpell, Geoffrey. **"Diamox" in the management of glaucoma.** M. J. Australia 2:846-850, Nov. 19, 1955.

Diamox is described as a potent inhibitor of carbonic anhydrase in the iris and ciliary body. It was used in the management of 20 cases of glaucoma. Its greatest value is in the treatment of acute rises of tension to lower the tension and quiet the eye for operation under favorable conditions. It is very useful in the management of glaucoma associated with uveitis or following central vein thrombosis. Diamox provides valuable adjuvant therapy to the previously established methods of treatment. (5 figures, 4 tables, 8 references)

Ronald Lowe.

Wagener, A. **A comparison between iridencleisis and the trephine operation.** *Klin. Monatsbl. f. Augenh.* 127:528-536, 1955.

In this comparison between 179 iridencleisis and 120 trephine operations there was no remarkable difference between the two series as far as visual acuity, field or intraocular pressure are concerned. There were no infections after the iris inclusion, but three late infections occurred after trephine. Lens opacities developed after iridencleisis in ten eyes and after trephine in 46 eyes. (32 references).

Frederick C. Blodi.

10

CRYSTALLINE LENS

Das Gupta, B. K., and Basu, R. K. **Bilateral dislocation of lens under complete voluntary control in Marfan's syndrome with cardiovascular anomaly.** *Brit. J. Ophth.* 39:566-568, Sept., 1955.

A 15-year-old girl with Marfan's syndrome had bilateral dislocated lenses which she could move into the anterior or posterior chamber by assuming a particular posture. One lens was small and cataractous, while the other was normal. The child showed some cardiac anomaly as well. The small cataractous lens was easily removed by surgery, but a detached

retina developed and it was decided to leave the second eye untouched. (2 figures, 17 references)

Morris Kaplan.

Papoleczy, F. **Cataract extraction in one-eyed patients.** *Klin. Monatsbl. f. Augenh.* 127:576-591, 1955.

Thirty-six such operations were done during the last 12 years; 10 of these cataracts were senile, the others were complicated. The extraction was intracapsular in 27 eyes and a total iridectomy had to be done in 16 eyes. Vitreous loss occurred in two cases. (4 references)

Frederick C. Blodi.

11

RETINA AND VITREOUS

Alajmo, Arnaldo. **Anatomo-pathological antagonism between pigmentary degeneration of the retina, and retinal detachment.** *Gior. ital. oftal.* 8:223-228, May-June, 1955.

After noting that there is no detailed description of cases of pigmentary degeneration of the retina associated with retinal detachment, the author observes that because of the pathologic changes seen in the former condition, separation of the retina would hardly be possible. (11 references)

V. Tabone.

Bailliart, P. **Isolated hypotension of the central retinal artery and its significance.** *Presse Med.* 63:1592-1593, Nov. 19, 1955.

Circumscribed orthostatic cerebral hypotension which is signalized by vertigo in the erect position or with change in the position of the head can be diagnosed definitely by the associated hypotension of the central artery of the retina during the attack, though the systemic blood pressure remains normal. In a typical case in which the intraocular pressure was 18, the diastolic pressure of the central retinal artery taken with the Bailliart dynamometer was only 20 after the onset

of vertigo while sitting up, but returned to its normal value of 40 after lying down. This functional circulatory derangement may perhaps be due to hyper-irritability of the carotid sinus. (21 references)

James E. Lebensohn.

Doden, Wilhelm. **The blood picture in retinal periphlebitis.** *Klin. Monatsbl. f. Augenh.* 127:416-422, 1955.

A group of 50 patients with retinal periphlebitis was compared with another group of 50 patients who had chronic uveitis. The red and white blood count, the differential count, the sedimentation rate and the prothrombin time were compared. In neither of the groups was there a significant deviation from the normal values. The only probable deviation was the erythrocyte count in the periphlebitis group. (2 tables, 47 references)

Frederick C. Blodi.

Dodo, T. **Diapupillary resection of vitreous opacity.** *Acta Soc. Ophth. Japan* 59:1737-1747, Nov., 1955.

In four cases of organized vitreous opacity, Dodo removed the lens and then cut off the organized opacity in the vitreous. In the first case, the vision was perception of hand movement despite all efforts to relieve it for six months. After the author's operation, a vision of 20/40 was restored in two months. After two years, the vision became 20/20. In the second case, the original vision was the same as in the first case for three years despite all efforts. After the operation, a vision of 20/50 was restored in four months. The third case had an original vision of 20/100. After the operation, a vision of 20/20 was obtained in two years. In the last case, the operation was not successful, as a secondary glaucoma resulted after the surgery. (10 figures, 1 table, 8 references) Yukihiro Mitsui.

Fischer, Franz. **Benign hypertony and**

ocular fundus. *Arch. f. Ophth.* 156:154-161, 1955.

In the study of 130 patients the author confirmed the experience that benign hypertension does not produce characteristic changes in the ocular fundus. (62 references) Ernst Schmerl.

Giacomelli, P. **Retinal hemorrhages in cases of myeloma.** *Gior. ital. oftal.* 8:255-263, May-June, 1955.

Two patients with different manifestations of myeloma in which retinal hemorrhages were a feature are described. The small literature is briefly reviewed. The disease affects all hematopoietic tissues, and the retinal hemorrhages result from the proliferation of cells around the retinal capillaries, which then become stenosed and finally rupture. (2 figures, 12 references) V. Tabone.

Givner, Isadore. **Present-day concept of diabetic retinopathy.** *Diabetes* 4:284-289, July-Aug., 1955.

The theories for the formation of diabetic retinal lesions are reviewed and brought up to date. Stress is laid on the recently discovered relationship of diabetes, excessive adrenocortical function, and relative vitamin B₁₂ deficiency in the production of retinopathy. Mention is made of the auxiliary plasma protein properdin, the discovery of which opened new vistas. In the discussion following, Wise stresses the early changes observed in venules. (11 references)

Harry Horwich.

Heer, Giuseppe. **Central scotoma in a case of occlusion of a branch of the central retinal artery.** *Rassegna ital. ottal.* 24:285-293, July-Aug., 1955.

The case of a man, aged 59 years, whose vision was reduced to 1/10 by a patch of retinal edema, resulting from occlusion of a papillomacular branch of the central retinal artery, is reported. The general

condition of the patient was good and the retinal vasculature showed little sclerosis. The patient also had a cilioretinal artery in the temporal quadrant. A colored drawing, a photograph and a diagram of the fundus clearly show the relationship between the vascular pattern and the area of edema and presumably of infarction in the fundus. (4 figures, 22 references)

Eugene M. Blake.

Jaeger, Wolfgang. **The etiology of a retinal disinsertion in the lower temporal quadrant.** *Klin. Monatsbl. f. Augenh.* 127:423-427, 1955.

This type of retinal detachment is frequently of traumatic origin and occurs in young patients. In about a fourth of the cases an isolated retinal cyst is present. Such detachment was observed in a 21-year-old man after a severe fall. Ophthalmoscopic examination of his relatives revealed that his father and two of his six siblings had definite pathologic findings. These patients showed a marked constriction, sheathing and even obliteration of the retinal arterioles in the lower outer segment. It is assumed that there is a familial disposition for this type of disinsertion. (2 figures, 5 references)

Frederick C. Blodi.

Lijo Pavia, Justo. **Improvement of degenerative macular diseases treated with cortisone.** *Rev. oto-neuro-oftal.* 30:85-88, May-June, 1955.

The author has used cortisone subconjunctivally or by intraorbital injection for the past three years in many different ocular diseases. He reports here his experience with a diabetic patient, with severe diabetic retinopathy and macular degeneration, and who showed a marked improvement in visual acuity with disappearance of macular lesions after three intraorbital and 10 subconjunctival injections of 10 milligrams of cortisone. The author emphasizes the antiinflam-

matory effect of cortisone. (3 figures, 11 references)

Walter Mayer.

Meyer-Schwickerath, G. **Light coagulation. A method for treatment and prophylaxis of retinal detachment.** *Arch. f. Ophth.* 156:2-34, 1954.

On the basis of observations of burns of the macula produced by sunlight, the author developed a method and apparatus for light coagulation. A special arc light was used and light rays were thrown upon the retina through the dilated pupil and under ophthalmoscopic guidance. A commercially available light cautery may soon be offered by the Zeisswerke in Oberkochen, Germany. So far experimental studies have demonstrated that satisfactory adhesions between retina, choroid and sclera can be produced. Clinical work showed that retinal holes in the macula or periphery can be closed. This was done in 40 patients before major detachments developed. A melanosis of the choroid was destroyed in one case. (11 figures, 36 references)

Ernst Schmerl.

Mikuni, S. **Blood pressure of retinal artery in some fundus diseases. I-V.** *Acta Soc. Ophth. Japan* 59:1359-1364, 1577-1603, 1645-1657, 1748-1753, Sept., Oct., Nov., 1955.

The results of a measurement by the Keio-type ophthalmodynamometer are given. According to Mikuni, the blood pressure of the central retinal artery is apt to be low in optic nerve atrophy, and the converse is true in optic neuritis. In both cases the capillary blood pressure at the macula is one half of that of the central artery and this ratio is normal.

In retinal angiosclerosis and retinal angiospasm, the ratio of the systolic blood pressure of the central retinal artery to the systemic pressure is higher than in normal and this ratio is 0.6:1.0; normally it should be 0.5:1.0. However, the ratio

of the capillary pressure at the macula to the pressure of the central artery is normal, and it is 0.5:1.0.

In albuminuric retinitis, the situation is converse. The ratio of the retinal blood pressure to the systemic pressure is normal (0.5:1.0), while the ratio of the capillary pressure at the macula to the arterial pressure is high in some cases.

In pigmentary degeneration of the retina, the capillary pressure at the macula is apt to be low; in central serous retinopathy, it is apt to be high. (12 figures, 26 tables, 171 references)

Yukihiko Mitsui.

Naunton, W. J., and Forrester, R. M. **Severe vitreous hemorrhage in a premature infant.** *Brit. J. Ophthalm.* 39:563-565, Sept., 1955.

Intraocular hemorrhage in the newborn does not occur as frequently as might be expected and almost no reports of vitreous bleeding in the newborn have appeared. In this case the mother, during delivery, became eclamptic after the head had been delivered and much spasm around the neck of the baby occurred. When the fundi were examined nine days later, hemorrhage was seen in the vitreous of one eye which became worse and appeared in the other eye three days later. After seven months the hemorrhage in each eye had disappeared almost completely. (6 references) Morris Kaplan.

Owens, W. C., Friedenwald, J. S., Silverman, W. A., Kinsey, V. E., Patz, A., Blodi, F. C., and Reese, A. B. **Symposium: Retrolental fibroplasia.** *Tr. Am. Acad. Ophthalm.* 59:7-41, Jan.-Feb., 1955.

Owens, W. C. **Clinical course.** pp. 7-10. This is ably described by one of the foremost investigators in this field. (2 figures)

Friedenwald, J. S. **Pathology.** p. 11. The author describes the minute tissue

changes from the 100 mm. stage to the late cicatricial stages.

Silverman, W. A. **Pediatric considerations.** pp. 12-14. The author discusses the variables in premature infants and points out the errors in assuming that all prematures are identical for a group or concerted study.

Kinsey, V. E., and Hemphill, F. M. **Etiology of retrolental fibroplasia and preliminary report of cooperative study of retrolental fibroplasia.** pp. 15-24. The authors list the cooperating investigators and present five tables and two graphs to illustrate the positive association between the incidence of the condition and the administration of oxygen. This is a preliminary report which concludes that the use of oxygen be restricted to minimal amounts required for the survival of the infant. (2 graphs, 5 tables, 18 references)

Patz, A. **Experimental studies.** pp. 25-34. Patz describes his experiments on anoxia in newborn mice and rats which support the clinical observation that oxygen is closely associated with the development of retrolental fibroplasia. (11 figures, 17 references)

Blodi, F. C. **Management.** pp. 35-38. The author describes the ophthalmoscopic examination during the active and cicatricial phases, complications, educational and social adjustment, and, counselling to the parents. (4 figures)

Reese, A. B. **Conclusions.** pp. 39-41. Reese suggests that every theory concerned with the etiology of retrolental fibroplasia has failed except that concerned with oxygen and that even with judicious use there will be occasional cases of retrolental fibroplasia. When oxygen is indicated, every effort should be made to keep the concentration below forty percent. Theodore M. Shapira.

Poos, Fr. **The pathogenesis of retinal detachments. Part II.** *Arch. f. Ophthalm.* 156:191-208, 1955.

The author continues his theoretical considerations (cf. *Am. J. Ophth.* 39:917) which do not easily lend themselves to condensation.

Ernst Scherml.

Puender, H., and Schmidt, K. H. **Ocular involvement in fat embolism.** *Klin. Monatsbl. f. Augenh.* 127:427-431, 1955.

Two patients were observed who developed whitish, isolated retinal foci after severe fractures. The lesions were bilateral and caused temporary visual impairment in one patient where they occurred in the macula. The lesions disappeared after a few weeks. Such fat emboli may be more frequent than is assumed. (46 references) Frederick C. Blodi.

12

OPTIC NERVE AND CHIASM

Marguart, Gisela. **Pseudopapilledema.** *Klin. Monatsbl. f. Augenh.* 127:546-558, 1955.

Seven cases with pseudopapilledema are described. Four patients had hyperopia (only one was severe) and two had myopic astigmatism. In the seventh patient drusen of the optic nervehead were present. Four more patients are described in whom the papilledema was part of a severe hypertensive retinopathy. (4 figures, 35 references) Frederick C. Blodi.

Stagni, S. **Treatment of chronic retrobulbar neuritis with retrobulbar injections of nicotinic acid.** *Gior. ital. oftal.* 8:335-347, July-Aug., 1955.

Retrobulbar injections of nicotinic acid were given with good results to 43 patients with chronic retrobulbar neuritis.

Visual acuity improved and scotomas became smaller. 11 mg. were given on alternate days, and the maximum number of injections was 20. (2 tables, 22 references) V. Tabone.

13

NEURO-OPHTHALMOLOGY

Frezzotti, R. **The localizing value of the Foster Kennedy syndrome.** *Boll. d'ocul.* 34:498-509, Aug., 1955.

The author adds to the literature the eighth case of "inverse" Foster Kennedy syndrome in which the tumor is located contralateral to the atrophic nerve. The author's patient was a 51-year-old woman with left optic atrophy and right papilledema. Initial left arteriography was negative, but right arteriography suggested an avascular tumor in the temporal pole area. Right frontal craniotomy revealed a meningioma of the lesser wing of the sphenoid on the right side. (1 table, 1 photograph, 16 references)

William C. Caccamise.

Genis Galvez, Jose M. **A case of myasthenia gravis with retraction of the lid.** *Arch. Soc. oftal. hispano-am.* 14:1412-1416, Dec., 1954.

The author adds a sixth case of retraction of the upper lid in myasthenia gravis to the five reported in the literature. The author's patient, a woman, 35 years old, had among other symptoms of myasthenia, a ptosis of the left upper lid, which improved with rest, and was accentuated by fatigue, and a retraction of the right upper lid, unaffected by rest or effort. (2 figures) Ray K. Daily.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 12th of the month. For adequate publicity, notices of post-graduate courses and meetings should be received three months in advance.

RESEARCH FELLOWSHIPS

The Department of Ophthalmology, Indiana University School of Medicine, is receiving applications for research fellowships in ophthalmology. These fellowships run for one year and may be renewed if mutually desired. The stipend is \$2,000.00 per year. Interested physicians, including foreign ophthalmologists with a knowledge of English, should apply to:

T. F. Schlaegel, Jr., M.D.,
Director of Research,
Department of Ophthalmology, Indiana University Medical Center,
1100 West Michigan Street,
Indianapolis 7, Indiana

CHANGES IN REQUIREMENTS

The American Board of Ophthalmology gives the following notice of changes in requirements applicable to applicants who start residencies in ophthalmology after December 31, 1956:

Individuals who have completed three years of formal ophthalmologic training (residency and basic science courses) may apply for the written qualifying test after completion of 12 months of practice or 12 months of institutional work, a total of 48 months. All other individuals (with less formal training) may apply for the written test after 60 months in ophthalmology or 72 months of combined ophthalmology and otolaryngology. A basic course is recognized as equivalent in time to residency training. All time requirements must be completed by the date of the written test.

COURSE IN GLAUCOMA

A seminar on glaucoma with particular emphasis on gonioscopy and the study of the anterior angle will be given at the Brooklyn Eye and Ear Hospital on May 21, 22, and 23, 1956. Ample opportunity for practical instruction in the use of the gonioscope will be given and material from the glaucoma clinic will be utilized.

The course will be given by Dr. Daniel Kravitz, assisted by Dr. Walter V. Moore, Dr. Mortimer A. Lasky, Dr. Harold F. Schilback, and Dr. Arthur Shainhouse.

Registration is limited to six ophthalmologists only.

Application and the fee of \$50.00 may be addressed to:

Dr. Daniel Kravitz
Brooklyn Eye and Ear Hospital
29 Greene Avenue
Brooklyn 38, New York

BASIC COURSE IN ORTHOPTICS

The basic course in orthoptics for technicians, sponsored by the American Orthoptic Council, will be held in the Department of Ophthalmology, University Hospitals, Iowa City, Iowa, from June 20 through August 11, 1956. As usual, there will be didactic lectures and practical demonstrations, given by an outstanding faculty.

Further information and application blanks may be obtained from:

Dr. Hermann M. Burian
Department of Ophthalmology
University Hospitals
Iowa City, Iowa

SIGHT-SAVING CONFERENCE

The 1956 sight-saving conference of the National Society for the Prevention of Blindness will be held March 26th, 27th, and 28th at the Palmer House in Chicago. Reports of new research into the causes of the blinding eye diseases will be made by outstanding ophthalmic investigators during the three-day sessions. Other highlights include the presentation of new techniques and procedures in various phases of sight-conservation work in the fields of medicine, education, nursing, social work, and safety. Many interesting related exhibits will be on display.

BRAZILIAN HOME-STUDY COURSES

Inspired by the home-study courses sponsored by the American Academy of Ophthalmology and Otolaryngology, the Hospital dos Servidores do Estado, Rua Sacadura Cabral 178, Rio de Janeiro, Brazil, will sponsor a home-study course designed for ophthalmologists. Each month a student will be mailed the printed matter concerning the subject of that month, with illustrations and bibliography. From the second month on questions regarding the subject of the preceding month with the correct answers enclosed in another envelope will make it possible for the student to give his own examination. The subjects covered will be:

April: Anatomy, histology, and embryology of the eye. May: Eye physiology. June: Eye examination. August: Refraction and ocular motility. September: Neuro-ophthalmology and ocular manifestations of systemic diseases. October: Eye diseases, pathology and treatment. November: Eye diseases and eye surgery.

Dr. Almiro Azeredo will be the director of the course.

SOCIETIES

LATIN SOCIETY CONGRESS

The 11 Congress of the Latin Society of Ophthal-

mology will be held in Madrid, Spain, from April 24 to 28, 1956. On the organizing committee are: President, Prof. Buenaventura Carreras; directors, Dr. H. Arruga, Prof. Diaz Caneja, and Dr. Lopez Enriques; secretary, Dr. Costi; assistant secretaries, Dr. Nier and Dr. Carreras Matas.

The special report to the congress will be "The use of acrylic material in ophthalmology." Dr. H. Arruga, Barcelona, will speak on "Orbital applications"; Prof. G. B. Bietti, Parma, Italy, on "Use in the surgery of the lids and lacrimal ducts"; Prof. L. Pauque, Lyon, France, on "Intraocular applications"; Dr. Olga Ferrer, Havana, Cuba, "Contact lenses"; Dr. Legrand, Nantes, France, "Intracorneal plastics."

Further information on the meeting may be obtained from:

Dr. Costi
Montalban 3
Madrid, Spain

IOWA MEETING

At the recent winter meeting of the Iowa Academy of Ophthalmology and Otolaryngology held at the University Hospitals, Iowa City, members of the Department of Ophthalmology spoke on:

"Arachnoiditis," Dr. Alson E. Braley; "Unilateral exophthalmos," Dr. P. J. Leinfelder; "Comments on a case of accommodative esotropia," Dr. Hermann M. Burian; "Mustard-gas keratopathy," Dr. Frederick C. Blodi; "Osler's disease," Dr. Philip Ellis.

At the luncheon business meeting, the following officers were elected for 1956: President, Dr. Carl Noe, Cedar Rapids; secretary-treasurer, Dr. Arthur C. Wise, Iowa City.

NASSAU MEETING

The Nassau (County, New York) Ophthalmological Society held its February meeting at Westbury. Dr. Bryon Smith, New York, spoke on "Plastic surgery: Preferred techniques."

OREGON ACADEMY MEETING

The 15th annual spring postgraduate convention of the Oregon Academy of Ophthalmology and Otolaryngology was held at the University of Oregon Medical School, Portland, March 19th to 22nd. The guest speakers were: Dr. Bernard Becker, Saint Louis; Dr. Samuel J. Kimura, San Francisco; Dr. Frank D. Lathrop, Boston; and Dr. Howard P. House, Los Angeles.

PACIFIC COAST MEETING

The 1956 meeting of the Pacific Coast Ophthalmological Society will be held at Phoenix, Arizona, April 15th to 19th.

BENGAL OFFICERS

The Ophthalmological Society of Bengal has the following executive committee: President, Capt. K. Sen; vice-presidents, Maj. E. J. Somerset and Maj. H. K. Indra; secretaries, Dr. S. Bagchi and

Dr. M. Sengupta; assistant secretaries, Dr. B. K. Mitra and Dr. G. Mukherjee; treasurer, Maj. V. P. Patel.

MIAMI OFFICERS

Officers for 1956 of the Greater Miami Eye, Ear, Nose and Throat Society are: President, Dr. A. R. Hollender; vice-president, Dr. Curtis D. Benton, Jr.; secretary-treasurer, Dr. James H. Mendel, Jr. The society meets quarterly in February, May, October, and December at the Seven Seas Restaurant.

AMERICAN GOITER ASSOCIATION

The 1956 meeting of the American Goiter Association will be held at the Drake Hotel, Chicago, on May 3rd, 4th, and 5th. The program will be devoted to papers and discussions on the physiology and diseases of the thyroid gland.

KANSAS CITY MEETING

Dr. Frederick C. Blodi, Iowa City, spoke on "Provocative tests for the diagnosis of early glaucoma," before a recent meeting of the Kansas City Society of Ophthalmology and Otolaryngology. Demonstrations of gonioscopy and tonography were also given at the eye clinic of the University of Kansas Medical Center.

Officers of the society are: President, Dr. Donald O. Howard; president-elect, Dr. Bernard C. Trowbridge; vice-president, Dr. Gunnar O. Proud; secretary, Dr. Dick Underwood; treasurer, Dr. James T. Robison, Jr.

MILWAUKEE PROGRAM

At the sectional meeting of the American College of Surgeons held at Milwaukee, Wisconsin, February 27th, 28th, and 29th, Dr. Erwin E. Grossmann, Milwaukee, presided at the luncheon for ophthalmologists and otolaryngologists. Moderator for the panel discussion on "Cataract surgery and glaucoma: Recent advances in glaucoma surgery," was Dr. Kenneth L. Roper, Chicago. Collaborators were Dr. Samuel Meyer, Chicago, and Dr. Harold G. Scheie, Philadelphia.

HAWAII OFFICERS

The officers of the Hawaii Eye, Ear, Nose, and Throat Society for 1956 are: President, Dr. Thomas W. Cowan; treasurer, Dr. Raymond Ogawa; secretary, Dr. Robert H. Lee. The society meets on the third Thursday of each month excepting July, August, and September. The meeting is generally a cocktail-dinner meeting and the society welcomes guests.

FRENCH SOCIETY CONGRESS

The 63rd congress of the French Society of Ophthalmology will be held in Paris from May 6th to 10th. The annual report will be given by Dr. M. Paul Bregeat on the subject of "Edema of the optic nerve." Two sessions will be devoted to (1) "Orbit, lids, and adnexa," and (2) "Optic nerve and amblyopia."

MIDWEST RESEARCH SECTION

The scientific session of the Midwest Section of the Association for Research in Ophthalmology was held in Chicago on March 17th. The program included:

Dr. Julia T. Apter, Manteno State Hospital, Manteno, Illinois: "The effect of hallucinogenic drugs on the electroretinogram" and "Studies on the autonomic innervation of the iris"; Dr. S. B. Goren and Dr. A. C. Krause, University of Chicago, Chicago: "Oxygen in the vitreous humor in anoxia and hyperoxia"; Dr. I. Gersh, University of Chicago, Chicago: "Electron microscopy of ocular tissues"; Dr. K. L. Chow, University of Chicago, Chicago: "Disuse and retrograde degeneration of retinal ganglionic cells"; Dr. E. S. Guzman Barron, University of Chicago, Chicago: "On the mechanism of oxygen poisoning."

Dr. N. P. Arribas and Dr. T. F. Schlaegel, Jr., University of Indiana, Indianapolis: "Experimental toxoplasmosis in the rabbit"; Dr. P. T. White and T. F. Schlaegel, Jr., University of Indiana, Indianapolis: "The results of photic driving on the electroencephalograms of patients with suppression amblyopia"; Dr. N. Kent and Dr. T. F. Schlaegel, Jr., University of Indiana, Indianapolis: "Selective perception in hysterical amblyopia." Dr. P. A. Cibis, M. Constant, and G. Pribyl, Washington University, Saint Louis: "Ocular lesions produced by iodoacetate"; Dr. R. E. Christensen and Dr. Bernard Becker, Washington University, Saint Louis: "The effect of Beta hypophamine on intraocular pressure and aqueous flow in human eyes"; M. A. Constant and Dr. Bernard Becker, Washington University, Saint Louis: "Experimental tonography; II. The effect of various compounds on the intraocular pressure of the rabbit."

Dr. R. D. Richards, State University of Iowa, Iowa City: "Histologic changes in radiation cataracts in mice"; Dr. M. Hobson Rice, State University of Iowa, Iowa City: "Familial occurrence of developmental anomalies of cornea, iris and chamber angle with visible region of Schlemm's canal"; Dr. C. Matta, State University of Iowa, Iowa City: "The skin test for moniliasis"; Dr. P. J. Hauser, State University of Iowa, Iowa City: "Studies on the fixation pattern in amblyopia ex anopsia"; Dr. F. C. Blodi, State University of Iowa, Iowa City: "Influence of newer ganglioplegics on the eye"; Dr. M. Armaly, State University of Iowa, Iowa City: "Comparison of bulbar pressure test and tonography."

F. W. Newell and Dr. T. Sheftel, University of

Chicago, Chicago: "Studies concerning the ocular hypertensive reaction following paracentesis"; Dr. G. J. Wyman, Peoria, Illinois: "Use of Versene in removal of rust in the cornea."

ORTHOPTIC EXAMINATIONS

The annual examination of orthoptic technicians by the American Orthoptic Council will be conducted in August and October, 1956.

The written examination will be nonassembled and will take place on Thursday, August 23rd, in certain designated cities. It will be proctored by assigned ophthalmologists.

The oral and practical examinations will be held on Saturday, October 13th, in Chicago just preceding the meeting of the American Academy of Ophthalmology and Otolaryngology.

Application for examination will be received to July 1, 1956, by the office of the chairman of examinations:

Dr. Frank D. Costenbader

1605 22nd Street, N.W.

Washington 8, D.C.

Applications must be accompanied by the examination fee of \$30.00. No application will be accepted after July 1, 1956.

PERSONALS

Dr. George M. Haik, New Orleans, was a speaker at the annual clinical conference of the Chicago Medical Society, held in Chicago February 28th and 29th and March 1st and 2nd. The subject of Dr. Haik's address was "Treatment of eye injuries."

Dr. Alston Callahan, Birmingham, Alabama, addressed the Bombay Ophthalmologists' Association at the October 30, 1955, meeting. Dr. Callahan also showed a film on "Surgery of the orbit."

Mrs. Helenor Wilder Foerster, now of San Francisco, was presented the Leslie Dana Gold Medal, awarded annually by the Saint Louis Society for the Blind to a person selected by the National Society for the Prevention of Blindness, at a dinner meeting in Saint Louis on January 26th.

Dr. Derrick Vail, Chicago, recently returned from a 30-day tour of the U. S. Army hospitals in Europe as a consultant in ophthalmology.

Dr. Paul A. Chandler, Boston, recently addressed the Section on Ophthalmology of the College of Physicians of Philadelphia. The subject of his address was "Surgery of congenital cataract: With special reference to complications of surgery."

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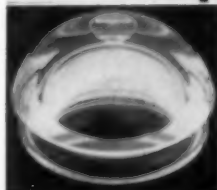


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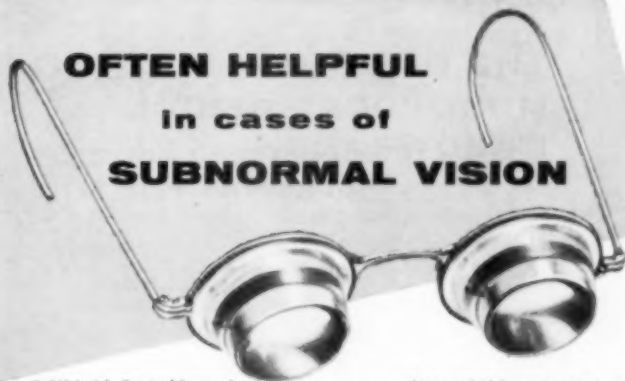
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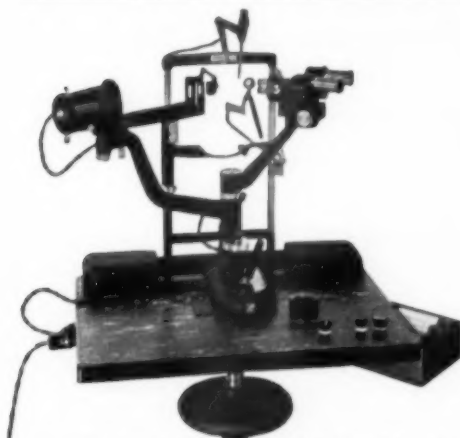
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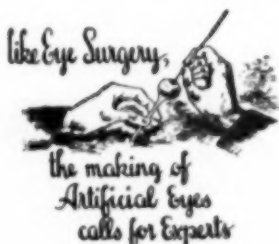
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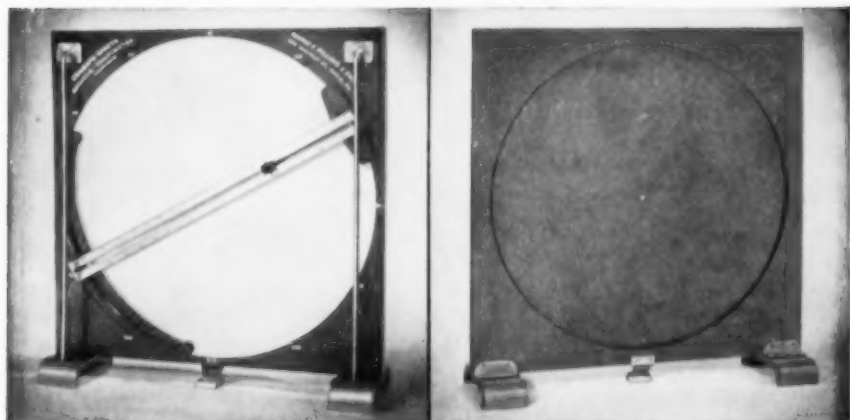
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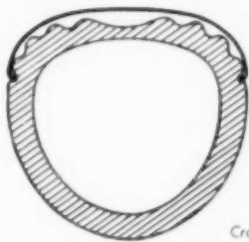


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